STUDIES ON THE EFFECTS OF *TRYPANOSOMA VIVAX* INFECTION ON OVINE PREGNANCY

BY

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DECLARATION

This work presented in this thesis is original and conducted under the supervision of Professors D. Ogwu, K.A.N. Esievo and E.O. Oyedipe in the Department of Surgery and Medicine, Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria.

It is a record of my research work and has not been presented before to any Institute or body for any award or honours.

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13th JANUARY 2000

Date

CERTIFICATION

This thesis titled "Studies on the effects of *Trypanosoma vivax* infection on Ovine Pregnancy, by Elias Kambai Bawa, meets the regulations governing the award of the degree of Doctor of Philosophy of Ahmadu Bello University and is approved for its contribution to scientific knowledge and literary presentation.

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DEDICATION

This Thesis is dedicated to the glory of our Lord Jesus Christ, for making it possible for me, despite all difficulties, to carry out this study to completion for the award of the degree of Doctor of Philosophy in Theriogenology.

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ABSTRACT

Three groups of six pregnant Yankasa and six pregnant West African Dwarf (WAD) ewes in each group, were assigned at random to first, second and third trimester of pregnancy study groups, for studies of the clinical manifestation of *Trypanosoma vivax* infection, the effects of the infection on pregnancy and the pathological lesions in the dam and foetuses. The effects of Novidium$^{(R)}$ (homidium chloride) chemotherapy intervention were also investigated. A group of 3 pregnant Yankasa and 3 pregnant WAD ewes served as the un-infected controls for the study.

The infection was mild in the Yankasa and WAD ewes infected in their first trimester, severe in the Yankasa than the WAD ewes infected in their second trimester. In the third trimester the infection was very severe in the Yankasa ewes, severe in three WAD ewes and mild in the remaining WAD ewes. The severity of the infection increased as pregnancy progressed in the Yankasa.

Fluctuating parasitaemia and pyrexia were observed in all the infected Yankasa and WAD ewes infected in the three trimesters of pregnancy. Anaemia was observed in all the infected ewes. Significant differences ($P<0.05$) were observed between the PCV values of the infected Yankasa and WAD ewes in the second trimester, when the infection was severe in both breeds. The WAD ewes in this study tolerated the anaemia due to the infection better than the Yankasa. Decline in body weights were observed in the infected Yankasa ewes in all the trimesters of pregnancy. Decline in body weights in the WAD ewes, were observed only in the second and third trimesters of pregnancy. The WAD ewes in the first trimester showed increase in body weights just as the uninfected control WAD ewes. Death due to the infection was observed in the Yankasa ewes in second and third trimester of pregnancy. Death due to the infection was observed in only one WAD ewe and

in the second trimester of pregnancy.

Low foetal weights were observed in the infected-untreated Yankasa ewes in the first, second and third trimesters of pregnancy. Partial and almost complete foetal resorptions were observed in the infected-untreated Yankasa in the first and second trimesters of pregnancy respectively. Abortions were observed in the infected-untreated Yankasa and WAD ewes, in the third than the second trimester of pregnancy. In the infected-treated Yankasa ewes, abortions of dead autolysed foetuses were observed in the first and second trimester. Abortion of a live foetus and a case of dystocia were observed in the third trimester. The susceptibilty of the Yankasa ewes to the infection increased as pregnancy advanced in the ewes.

Embryonic death and resorption were observed in the infected-untreated WAD in the first and second trimesters of pregnancy. Abortions of live foetuses were observed in the third trimester. The infected-treated WAD ewes in the second and third trimester of pregnancy carried the pregnancies to term and delivered healthy lambs, in contrast to the Yankasa.

Pathological lesions in the ovaries, pituitary glands, liver, kidneys and lungs, observed in the Yankasa and WAD ewes infected in the first and second trimesters of pregnancy were similar, but differed in severity as influenced by the severity of the infection and breed of the ewe. Most severe lesions were observed in the second trimester, when the infection was severe and in the Yankasa than in the WAD ewes. Resolutions of the gross and histopathological lesions observed in the dam, subsequent to treatment were early in the infected-treated Yankasa and WAD ewes in first trimester of pregnancy, when the infection was mild. They were delayed or incomplete in the second trimester when the infection was severe and in the Yankasa than in the WAD ewes . The success of

chemotherapy in resolution of the pathological lesions in the ewes, was influenced by the severity of the lesions(due to the severity of the infection) at the time of treatment and the breed of ewe.

In this study chemotherapy with Novidium(R) at l.Omg/kg body weight, ameliorated the pathogenic effects of *Trypanosoma vivax* infection on gestation and delivery in the WAD ewes. It was therefore concluded from this study that if the trypanololerancc of WAD ewes is augmented with trypanocidal drugs chemotherapy, the productivity of the WAD sheep may be enhanced in areas endemic for trypanosomosis.

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CHAPTER ONE

INTRODUCTION

1.1 GENERAL INTRODUCTION

Livestock population in Tropical Africa was estimated at 161 million cattle, 264 million small ruminants(Jahnke,1982),12 million Camels, 12 million equine, 10 million pigs and 460 million chickens(Jahnke *et al.*,1987). Large ruminants, excluding camels, constitute 82% of the total tropical livestock units (TLU)[1]. They are by far the most important livestock species in Tropical Africa (Jahnke *et al.*, 1987).

The livestock industry in Nigeria contributes substantially to the National wealth and also supplies the population with important animal protein required for healthy living. In addition, it provides raw materials for the related agro-based industries and plays a significant role in promoting crop production through use of animal traction and manure for soil fertility. Livestock also plays important cultural roles (David West, 1985).

Livestock population in Nigeria in 1992 was 13,885,813 million cattle, 22,092,602 million sheep and 34,453,724 million goats (Rim, 1992 report). This represent an increase in livestock numbers from 1972 figures which stood at 11.41 million cattle, 8.0 million sheep and 23.5 million goats. Despite this increase, the targeted supply of animal protein according to the livestock perspective plan (1991-2002) of 16.36 g/head/day has not been attained.

The animal protein offtake from Nigerian livestock has been estimated to provide less than 50% of the FAO, recommended target of 35.0gms/caput/year of animal based proteins (David West, 1985).

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[1] Tropical livestock unit is taken to be an animal of 250 Kg live weight.

Nigeria is endowed with huge livestock resources, the majority of these animals are kept under traditional livestock management systems. Reports by Pullan (1979); Eduvie,(1985); Otchere, (1986); Otchere *et al*.,(1987); Voh and Otchere (1989) have shown that ruminants in Nigeria kept under traditional management systems have lower productivity compared to those kept in Government ranches and other institutional farms. It is therefore, evident that the low level of animal protein production in Nigeria is not as a result of numbers of animals, but their poor productivity due to management and disease factors.

Trypanosomosis which occurs across more than a third of Africa has been described as the most important livestock disease in the continent of Africa (ILRAD, 1990). The wide appearance of the disease in people and their livestock is a great constraint to agricultural and economic development with a consequent reduction in the welfare of the rural populace.

The tsetse fly (Glossina) vector of trypanosomosis occurs only in Africa. It is estimated that the disease is found in 37 countries of Africa, covering an area exceeding 10 million km^2. The risk of trypanosomosis in most of these areas threatens farmers from keeping cattle and small ruminants. This largely accounts for Africa's low livestock productivity. Africa produces one-seventeenth of animal protein per one hectare, compared to the quantity Europe produces, despite the abundance of livestock in Africa than Europe (ILRAD, 1990).

Most of the agriculturally productive areas of Africa are infested by tsetse flies, thereby making the impact of trypanosomosis on livestock even greater. Thirty percent of Africa's cattle population, totaling 147 million (ILRAD,1990), as well as comparable numbers of small ruminants are at risk from the disease.

Trypanosomosis had previously not been considered an important disease in small ruminants (Kramer, 1966; Maclennan, 1970; Stephen, 1970). However, studies have shown that these animals can be severely affected by this disease, resulting in heavy losses (Ikede and Losos, 1975; Griffin, 1978; Griffin and Allonby, 1979a,b; Saror, 1980). Nomadic herdsmen in Nigeria graze both cattle and sheep together in tsetse endemic areas, consequently both species of livestock are equally exposed to trypanosome infection. However, efforts in the country at controlling trypanosomosis have mainly focussed on bovines, despite the fact that small ruminants provide a very important source of meat protein for human consumption, most especially in the rural communities.

Annual losses in meat production are estimated at US $5.0 billion. This is further exercabated by losses in milk yield, tractive power, waste products that provide natural fuel and fertilizer and secondary products such as hides. In addition 50 million people are currently exposed to the risk of contracting human trypanosomosis (ILRAD, 1990).

Various breeds of livestock have been recognized to be tolerant to trypanosomosis thereby enabling them to survive and reproduce in areas endemic for trypanosomosis where other breeds would succumb to the infection (ILRAD, 1979). Trypanotolerant breeds of livestock in West Africa include the West African short horn cattle (Muturu and Ndama) and the West African Dwarf sheep and goats. The resistance of these breeds to trypanosomosis is not absolute. They can come down with the infection under stress conditions such as work, pregnancy, nutrition, parturition, lactation and intercurrent diseases (Desowitz, 1959; Murray *et al.*, 1982; Ogwu, 1983; Reynolds and Ekwuruke, 1988). Margaret *et al.*,(1988) reported that although trypanotolerant breeds of cattle are more resistant to trypanosomosis than the Zebu breed, a spectrum of susceptibility cuts across the two breeds. Similar observations have also been reported in Trypanotolerant

West African Dwarf and Yankasa sheep (Bawa *et al.,* 1990). Reproductive efficiency of Nigerian small ruminants have been shown to be affected by trypanosomosis (Adenowo, 1989; Reynolds and Ekwuruke, 1988; Bawa *et al.*, 1990). In addition, their response to the infection is also influenced by level of nutrition, stress due to pregnancy, work, and intercurrent diseases(Reynolds and Ekwuruke, 1988) .

The effects of Trypanosomosis on female reproduction of the various breeds of cattle (Murray *et al.*, 1981; Ogwu *et al.*,1986; Ogwu and Njoku, 1987); buffalos (Lor *et al.*, 1986); sheep (Adenowo, 1989; Bawa *et al.*, 1990); goats (Luckins *et al.*, 1986; Llewelyn *et al.*, 1988; Mutoyaba *et al.*, 1988a; Akinbamijo *et al.*, 1994),have been reported. The comparative effects of *T. vivax* infection on non-pregnant Zebu heifers and pregnant Zebu heifers at different stages of pregnancy have also been reported by Ogwu and Njoku (1987). There is however a dearth of information on the comparative effects of *T. vivax* infection on pregnant Yankasa and West African Dwarf sheep, the predominant breeds of sheep found in the main ecological zones of Nigeria, the semi-arid and humid zones, respectively. This study was therefore planned to:-

1. Compare the clinical manifestation of *T. vivax* infection on pregnant Yankasa and West African Dwarf Sheep.
2. Determine the effects of *T. vivax* infection on first, second and third trimester of pregnancy of Yankasa and West African Dwarf (WAD) ewes.
3. Evaluate the effects of treatment with Novidium(R) (Homidium chloride) at 1.0 mg/kg. body weight on the resolution of pathological lesions in the dam and foetuses.

CHAPTER TWO

LITERATURE REVIEW

2.1 SMALL RUMINANTS:

Small ruminants(sheep and goats), form part of nearly all farming systems in Nigeria. They have long been associated with Nomadic pastoralism, mixed farming systems, shifting cultivation and fallow, small holders farms and even among non farming communities, where they are tethered and fed in backyards(David-West, 1985).

They are widely distributed in the country with varying socio-economic functions, and are the favourite slaughter animals during festivities. They are also sources of financial investments used in times of need (Adu, 1980; David-West, 1985).

2.1.1 SHEEP:

Sheep play an important role in the socio-economic life of many Nigerians. They also contribute significantly to the national economy. Sheep kept mainly for mutton account for about 48,000.0 metric tons(11.0%), of total meat supply in Nigeria per annum(Adu and Ngere, 1979).

i. Population and Distribution of sheep in Nigeria:

Estimated sheep population ranged from 7.24 millions in 1963 to 25.0 millions in 1992 (Rim, 1992). Sheep are widely distributed in Nigeria, the areas of highest sheep breeds concentration are shown in Fig 2.1. These fall within the Sudan and Guinea Savanna zones of the country.

Fig.2.1. Areas of largest sheep breed concentration and major vegetation zones in Nigeria.(WAD=West African Dwarf Ewes(source Adu and Ngere(1979).



ii. Breeds of Sheep and Reproduction:

The indigenous sheep breeds in Nigeria can be broadly grouped into large, long-legged types found in the Northern parts of the country and the dwarf types of the humid coastal areas (Adu and Ngere, 1979). Four main breeds of sheep are found in Nigeria which are also adapted to the particular vegetation zones where they are found. The breeds are the Yankasa, Uda and Balami predominantly found in the Northern parts of Nigeria and the West African Dwarf(WAD) breed found in the southern area of the country.

a. Yankasa Breed:

They are kept predominantly by the Hausas. The Yankasa is widely distributed in the Northern parts of Nigeria. It is typically white with black patches around the eyes, ears, muzzle and sometimes the feet. The rams have curved horns and heavy hairy white mane. Some of the ewes have tassels on the neck, matured ewes weigh 25-40kg, while rams weigh 35-50kg (Adu and Ngere, 1979).

a.i. Reproduction in Yankasa:

The Yankasa ewe breeds throughout the year. The ewe attains puberty at the age of 34 weeks(Osinowo, 1989); age at first estrus is 5-7 months (Nuru, 1985); 8.0 months (Ojo *et al.*,1981), while estrous cycle length is 16.4 days (Osinowo, 1989).

The live weight of the Yankasa ewe at first estrus has been reported as 11-18kg (Nuru,1985), 21.8 $\pm$ 3.4kg (Adu and Ngere 1979), while the gestation period is reported as 151.4 days (Osinowo, 1989).

The post-partum interval to estrus has been reported as 34.3 days, while the post-partum interval to conception is 42.5 days (Osinowo, 1989). The lambing rate, weaning and litter size have been reported as 89.6%,79.2% and 1.26 respectively (Osinowo, 1989).

b. WAD Breed:

The WAD breed has been described as Fouta Djallonke (Mason,1951). In Nigeria, it is variously called the southern forest sheep (Orji *et al*., 1977), the Nigerian dwarf sheep (Adu, 1972; Orji, 1985). The breed is widely distributed in the area south of latitude 14^{0}N. The WAD sheep is a small, compact and hardy breed with a wide range of coat colours. It is very alert in appearance, thrives and breeds successfully all year round in areas infested with tsetsefly. This lends credence to the notion that the breed is trypanotolerant (Adu and Ngere, 1979).

b.i Reproduction in the WAD:

The WAD ewe attains puberty at 267.2(172-378) days (Orji and Steinbach,1980a,b), age at first estrus is 267.2 days (Orji, 1976), 5-6 months (Nuru, 1985), while estrous cycle length is 18.5 days (Orji and Steinbach, 1979). The live weight of the WAD ewe at first estrus has been reported as 13-16kg(Nuru, 1985), while gestation period is 142-153 days (Orji and Steinbach, 1980a,b) and age at first lambing 424.9(310-692) days (Orji *et al*., 1976); 10-22 months (Nuru, 1985).

The post-partum interval of the ewe has been reported as 248 days, while litter size and lamb survival are reported as 1.3 and 0.78, respectively (Nuru,1985).

iii. Sheep production systems:

The production systems of sheep vary from nomadic to sedentary and can be grouped into three systems that are closely related to the farming and cultural life of the people (Adu and Ngere, 1979; Adu, 1980). The three systems are:-The Nomadic Fulani system, the Hausa intensive compound system and the Government and Research farms *semi-intensive system*.

Otchere and Kallah(1990), grouped small ruminants management into three broad groups:- Extensive, Semi-intensive and Intensive. The three systems described by Adu and Ngere (1979) fall within the three groups of small ruminants management by Otchere and Kallah (1990).

a. Extensive system:-

This system is practiced nation wide. It is the same as the Nomadic Fulani system of sheep management described by Adu and Ngere(1979). In this system, sheep are grazed together with cattle throughout the year, moving from North to south of the country and vice versa in response to rainfall pattern and availability of pastures (Adu and Ngere, 1979).

After the day's grazing with cattle, the sheep are held by the neck loops to a rope tied between two pickets called `dangwali'. Shelter is not provided to the sheep under this system of management. They are exposed to rains during the rainy season (Otchere *et al.*, 1987; Otchere and Kallah, 1990).

In the southern parts of Nigeria, the extensive management system is the common practice of sheep production. Sumberg (1985), reported that the majority of the sheep and goats in South-West Nigeria, were kept in free roaming village flocks. The animals are left to graze and browse roadside herbage and are sometimes offered kitchen wastes, like cassava, yams or plantain peels. In the South-East of Nigeria, some flocks roam freely all year round, while others are controlled and kept within the compounds, to avoid crop damage during the cropping season. In Imo and Anambra, there is partial control of the animals due to increasing intensity of agricultural land use (Francis, 1988).

Under the extensive management system, animals are not provided with any housing, but spend the night in streets, motor roads, porches of houses or tied to dangwali (Adu and Ngere, 1979; Otchere and Kallah, 1990). Health care is poor under this system,

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breeding is not controlled, records are virtually non-existent and productivity in terms of lambing rate and lambs survival is low.

b.Semi-intensive System.

Natural grazing is the backbone of this system. Restriction of indiscriminate movement of sheep is imposed and this is directly related to the intensity of agricultural land use. Adu and Ngere (1979) reported that WAD sheep in the southern parts of Nigeria are kept in compounds and given supplementary feeding of chopped cassava roots, plantains, cassava peels, grains and herbage during the wet cropping season or are tethered on fallow fields.

In the dry season when there is no farming, the sheep are generally left to roam in the day, browsing on road side herbage and consuming kitchen wastes like yams and plantain peels(Adu and Ngere, 1979). Mack *et al.*(1985) reported that restriction of movement of sheep and goats in the south Eastern Nigeria was dictated by the production environment.

In the North, sheep are left to roam about in the dry season and spent the night tied by neck loops to "dangwali" or tied by the legs to pegs in huts in the compounds by the Hausa communities. During the wet season the sheep are fed by the "cut and carry system",. They are also supplemented with grain offal and on crop residues such as groundnut haulms, cow pea haulms and husk. Occasionally cotton seed cake is fed to them. Kanwa(local potash), serves as source of minerals. Housing is not provided, health care is poor, breeding is not controlled and records are hardly kept.

c.Intensive System.

Sheep that are traditionally kept intensively are fed under total confinement and provided with shelter against heat or cold stress, washed and brushed routinely. Shelters are

kept clean almost every day. This type of management is practiced as a secondary occupation by urban dwellers rather than pastoralist or agro-pastoralist. The system is adopted by these classes of people for fattening of rams for sales during Muslim festivities(Otchere and Kallah, 1990).

The Government and research farms systems of sheep management have been described as semi-intensive (Adu and Ngere, 1979). In this system the sheep are better managed. They are provided with good housing , better feeding and health care. Health care consist of routine de-worming, spraying or dipping for control of endo-, ecto- and haemo-parasites. Animals are grazed on improved pastures, while hay and silage is fed to the animals in the dry season. Supplementary feeding in form of compounded concentrate mixture of maize and cotton seed cakes are fed to the animals both in the dry and wet season.

The productivity of sheep under this system of management is better compared to the Nomadic Fulani and Hausa compound systems(Adu and Ngere, 1979). Otchere *et al.*(1987) and Voh and Otchere (1989) reported that ruminants in Nigeria kept in Government ranches and Research Institutes have higher productivity than those kept under traditional management systems.

iv. Economy of production:

In the extensive management system, the average flock size per household rarely exceeds 20. Inputs into production are low. Housing, supplementary feeding with concentrates, and health care are not provided. Labour input is usually household labour. Invariably outputs from this system of production are low. However the system is still profitable[Osinowo, 1986).

In the semi-intensive/intensive systems, inputs are high due to high stocking rate, provision of housing, supplementary feeding, health care, hired labour and administration. Supplementary feeding, salaries and wages constitutes the greatest items of expenditure. Formulation of least cost rations may reduce operating cost significantly. Osinowo (1986) reported that it is advantageous to operate a high stocking rate for this system of management to be profitable. He reported that the intensive farming under Nigerian conditions may only be profitable at a stocking rate of 15 breeding ewes per hectare of land, with twice yearly lambing. Under these conditions, 18.0% return on investment may be expected over a ten year period.

v. Trypanosomosis in sheep:

Trypanosomosis is one of the most important diseases of livestock in sub-Saharan Africa. It affects all livestock species including game animals. The wide occurrence of the disease have been reported to retard agricultural development (Stephen, 1966; ILCA, 1984). The major economic impacts of trypanosomosis on livestock has been through decreased growth rate, debilitation, delayed puberty and reduced milk production(Jeffcoate and Holmes (1997). The effects of trypanosomosis on reproduction are often compounded by the ill-effects of under-nutrition and concurrent disease (Reynolds and Ekwuruke, 1988).

Although the major economic impact of trypanosomosis is on cattle production, the disease also severely affects small ruminants, throughout sub-Saharan Africa(Jeffcoate and Holmes (1997). Studies on indigenous sheep in Nigeria have shown that reproductive efficiency of these animals is severely affected by trypanosomosis.

Various grades of abnormal estrus, such as silent estrus, irregular estrus and temporary or complete anestrus, have been reported in *T. vivax*, infection in Yankasa ewes (Adenowo, 1989) and WAD sheep (Elhassan, 1987). Abortions, still births, and birth of

weak lambs have also been reported in *T. vivax,* infected pregnant Yankasa ewes in second and third trimester of pregnancy (Bawa *et al.*,1990) and in WAD sheep infected with *T. vivax,* in the first and third trimesters of pregnancy (Elhassan, 1987). In the WAD sheep infertility and sterility have been reported in WAD sheep infected with *T. vivax*(Isoun and Anosa, 1974b). Low birth weights and survival rates have also been reported in WAD sheep infected with *T. vivax,* in middle pregnancy (Akinbamijo *et al.*, 1994). Reynolds and Ekwuruke (1988) also reported low birth weights and premature births of lambs in WAD ewes infected with *T. vivax, in* late pregnancy. A case of foetal mummification and death of ewe have also been observed in WAD ewes infected with *T. vivax,* in second trimester of pregnancy (Bawa *et al.*,1990).

Pathogenic trypanosomes have been demonstrated in amniotic fluid of pregnant sheep infected with *T. vivax* indicating transplacental infection (Isoun and Anosa, 1974a). Similarly Ikede and Losos (1972), reported transplacental infection of lambs with *T. vivax. T. brucei sp.* have been reported to cross the placenta, resulting in the death of the neonate and abortions in pregnant sheep (Edeghere *et al.*,1992).

Effects of trypanosomosis on reproductive organs of sheep, include ovarian cystic degeneration(Isoun and Anosa, 1974b). Adverse effects on endocrine organs of sheep have also been reported in *T. vivax* infection, leading to irregular progesterone production manifested in three types of abnormal estrus, namely silent estrus, temporary anestrus and complete anestrus. Lesions of the anterior pituitary, have been reported in sheep infected with *T. brucei (*Ikede and Losos, 1975).

Depression of progesterone production have been reported in sheep infected with *T. vivax* (Elhassan *et al.*, 1991). Ikede and Losos (1975) reported that trypanosome of the brucei group can cause widespread degenerative lesions in cattle, sheep and goats,

including the pituitary, thyroid and adrenal glands, accounting for the abnormalities observed in endocrine production in infected sheep.

2.2 TRYPANOSOMOSIS ON ANIMAL REPRODUCTION

i. Male Reproduction:-

The pathogenic trypanosome are described into vascular or extravascular forms [Losos and Ikede, 1972]. The vascular forms which include *T. vivax* and *T. congolense*, lodge in the capillaries where they attach to the endothelium and rarely leave the blood stream [Banks, 1978]. They have not been generally associated with extensive tissue damage (Jeffcoate and Holmes, 1997).

The extravascular trypanosome, the *T. brucei* group can cause wide spread degenerative lesions in the pituitary gland, thyroid and adrenal cortex of cattle, sheep and goats (Ikede and Losos, 1975). They are shown to invade the testis causing formation of granulomata and resulting in atrophy of the seminiferous tubules, complete disruption of spermato- genesis (Ikede, 1979; Losos, 1986) and degeneration of the testicular excurrent ducts. This may in part, reflect damage to the blood/testis barrier.

Infiltration of lymphocytes and macrophages into the testicular interstitium has also been observed in *T. brucei*-infected calves [Moulton and Sollod, 1976]; *T. brucei* infections in rams [Ikede, 1979] and *T. brucei* infections in boars [Omeke and Onuora, 1992]. The effects of trypanosome an the testis probably affects Leydig cell steroidogenesis and may explain reduced libido in infected cattle [Sekoni *et al.*, 1988].

Extensive testicular lesions have been described in *T. brucei* infections in rams [Ikede and Losos, 1972], *T. vivax* infections in sheep and goats [Isoun and Anosa, 1974b; Anosa and Isoun, 1980] and in *T. congolense* infection in goats [Kaaya and Oduor-Okelo, 1980; Waindi *et al.*, 1986]. Increased scrotal diameters, scrotal inflammations, scab

formation with alopecia as well as peri orchitis, epididymitis, severe testicular degenerations, abnormal spermatogenesis/aspermatogenesis and preputial haemorrhages have been reported in rabbits infected with *T. brucei* [Ikede and Akpavie, 1982]. Severe testicular degeneration have also been reported in *T. brucei* infections in mice [Anosa and Kaneko, 1984]. Genital lesions including gonadal atrophy have been described in *T. brucei* and *T. congolense* infections in Landrace white cross-bred boars [Omeke and Onoura, 1992].

Some of the effects of trypanosome on the male gonads are through the indirect effects of pyrexia, accompany waves of increasing parasitaemia during trypanosome infection [Mutayoba *et al.*, 1995b] and these are associated with increased scrotal temperature. Testosterone synthesis and secretion may be altered due to circulatory changes in the scrotum and testis as a result of elevated body temperature and the inevitable reduction of the temperature gradient between testis and body [Jeffcoate and Holmes, 1997].

Progressive decrease in circulating testosterone concentration has been reported in sheep infected with *T. congolense* [Adeyemo *et al.*, 1990; Mutayoba *et al.*, 1995a], decreased plasma testosterone has been described as a likely contributory factor in the reduced libido and azoospermia observed in clinical *T. congolence* infections [Ikede *et al.*, 1988]. Soudan *et al.*,(1992) implicated Leydig cell LH receptor desensitization in reduced testosterone levels following trypanosome infections.

Mutayoba *et al.*,(1994) observed marked deficiencies in gonadal testosterone secretion by 8 weeks following *T. congolense* infection in rams. The Leydig cells also showed reduced responsiveness to both human chorionic gonadotrophin (HCG) and the steroid precursor 22 R-hydroxy-cholesterol [22-ROGC]. The lack of response to 22-ROHC

implies deficiencies in the steroidogenic pathway [Jeffcoate and Holmes 1997].

Decline in testosterone as well as LH have been described in rams infected with *T. congolense*. From endocrine point of view as testosterone decline, LH would be expected to increase reflecting the declining negative feedback influence of testosterone on the hypothalamo-pituitary axis. The decline in LH probably indicates effects of trypanosome an the hypothalamo-pituitary axis [Jeffcoate and Holmes, 1997].

Endocrine studies have shown that *T. congolense* infection decreases plasma LH secretion from the anterior pituitary, through a mechanism which does not directly affect the pituitary gland but through one which either alters hypothalamic secretion of Gn/RH or reduces transport of Gn/RH to the pituitary in the hypophyseal blood vessels [Mutayoba *et al.*, 1994]. The suggestion that Gn/RH transport to the pituitary is reduced by trypanosome infections agrees with findings of reduced LH pulse amplitude in castrated infected rams [Jeffcoate and Holmes, 1997] and is supported by Abede *et al.*,(1993a,b) demonstration of significant changes in the microvasculature of the pituitary gland of cattle infected with *T. congolense*. These include blockage, vessels dilation and thickening of the extracellular matrix, such changes that are likely to interfere with Gn/RH transport or access to the pituitary gonadotrophs.

Another possible mechanism for trypanosome effects on the endocrine control of reproduction is an interaction with the glucocorticoids. Cortisol, which is an indicator of stress in many diseases has been shown to increase soon after *T. congolense* infection in rams [Mutayoba *et al.*, 1995b], goats [Mutayoba and Gombe, 1989] and cattle [Ogwu *et al.*, 1992]. High levels are described to reappear with subsequent waves of parasitaemia.

Cortisol has been shown to suppress pituitary gonadotrophin secretion in sheep [Naylor *et al.*, 1990] and cattle [Johnson *et al.*, 1982], by an effect on the pituitary

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gonadotrophins. In addition, cortisol is known to inhibit testosterone secretion by an effect an Leydig cell LH reception [Bambino and Hsuch, 1981].

ii. Female Reproduction:

Reports on the effects of extravascular trypanosome on female reproduction include *T. brucei* infection of pregnant ewes and cattle causing abortion and also crossing the placenta and resulting in the death of the neonate [Ogwu and Nuru, 1981; Edegbere *et al.*, 1992]. Many of the reports of naturally occurring and experimental trypanosomosis on female reproduction have been on *T. congolense* and *T. vivax*.

Anoestrus of up to 6 months haven been reported in Zebu heifers chronically infected with *T. vivax* [Ogwu *et al.*, 1984], while anoestrus of up to 100 days have been observed in boran cattle infected with *T. congolense* [Luckins *et al.*, 1986., Llewenlyn *et al.*, 1988]. Depressed conception rates in cows have also been observed [Fio-Ngaindiro, 1987]. Mutayoba *et al.*,(1988a) described increased numbers of small and antral follicles and occasional cystic follicles in infected goats with *T. congolense*, consistent with history of anoestrus.

Reproductive problems such as abortions during various stages of pregnancy, birth of weaklings, premature births, births of anaemic offspring, low birth weights and neonatal calf mortalities have been described in *T. vivax* and *T. congolense* infected cattle (Boyt, 1971; Ogwu *et al.*, 1986; Fio-Ngaindiro, 1987; Ogwu and Njoku, 1987; Anene *et al.*, 1991].

Ovarian function has been reported arrested with no functional structure in ovaries of *T. vivax*, infected Zebu heifers [Ogwu *et al.*, 1984]. Atrophic ovaries with multiple follicular cystic degeneration and total absence of corpora lutea in Zebu heifers have similarly been reported [Ogwu and Njoku, 1991].

The haematic trypanosomes have been shown to have far reaching effects on female reproductive organs and functions despite the fact that they are seldom identified in the tissues of the reproductive organs. This suggest that there may be indirect effects of the haematic trypanosome on reproduction in the female.

Mutayoba *et al.*(1988b,c) reported in goats the likelihood of partial luteinization of follicles at ovulation or reduced ovulation rate which is linked with low preovulatory oestradiol concentration. Resulting in lower than normal luteal phase progesterone and subsequent anoestrus. In another study in goats infected with *T. congolence*, elongated luteal phase progesterone level dominated the estrus cycle, resulting in persistent diestrus [Llewenlyn *et al.*, 1987].

Mutayoba *et al.*(1989) observed persistently elevated circulating prostaglandin metabolite levels in *T. congolense* infected goats. These were associated with reduced progesterone levels, short cycles and eventual anoestrus, suggesting that prostaglandins might be the cause of cyclic disturbances.

Pituitary gonadotrophin secretions are expected to be reduced in trypanosome-infected female ruminants as has been shown in males, particularly in view of the demonstration of lesions in infected females [Mutayoba *et al.*,1988a]. Reduced gonadotrophin support would therefore explain the degenerative changes in ovarian follicular development and also deficiencies in the ovulatory process such as cystic ovaries and follicular luteinization in infected animals, since corpus luteum of ruminants require luteolytic support in form of LH[Jeffcoate and Holmes, 1997].

Pyrexia have also been incriminated as having detrimental effects on ovarian and tubal function [Ogwu *et al.*, 1984]. Abortions observed in pregnant WAD ewes infected with *T. vivax* in first and third trimesters of pregnancy have been associated with the

pyrexia observed in the infected ewes (Elhassan, 1987); pyrexia has been described to alter the milieu interior of the uterus (Hafez, 1968), thereby making the uterus hostile to the foetus and expelling it. Also stress induced by pyrexia activates foetal hypothalamo-pituitary adrenal axis to produce corticosteroids from the foetal adrenal gland [Tilton *et al.*,1972]. These corticosteroids stimulate the production of PGf2-alpha and oestrogen from the placenta. The PGf2-alpha initiates abortion by reducing myometrial activity threshold, through reduction in concentration of progesterone, while oestrogen causes uterine contraction and foetal expulsion [Liggins *et al.*,1972].

Genital lesions have been described in female animals infected with trypanosome. Flaccidity and atony of the uterine horns have been reported by Ogwu *et al.*,(1984). Congestion with focal areas of haemorrhages have been reported in the uterine tubes of mice, rats and rabbits infected with *T. evansi* [Patel *et al.*, 1983]. The significance of these, is that conception may be impossible, through the occlusion of the tiny lumen, through acute or proliferative swelling [Jones and Hunt, 1983]. The swelling may destroy the ciliated epithelium or contractile muscles which propel the ovum to the uterus. Also, spermatozoa could be destroyed by toxins from the inflammatory exudates. Moulton and Sollod [1976] described oedema of the uterus of *T. brucei*-infected cattle, characterized by perivascular infiltration of the endometrium and between the circular and longitudinal muscle with lymphocytes, plasma cells and eosinophils. Diffuse infiltrations of mononuclear cells and solitary lymph follicles with active germinal centers were also observed beneath the endothelium.

Ogwu and Njoku (1991), described massive endometrial mononuclear cells infiltration, glandular atrophy, peri-glandular cell infiltration, myometrial atrophy and fibroplasia in the uteri of *T. congolense* infected Zebu heifers.

Lesions observed in the vulva of infected female animals, include transient oedema in the vulva of a Zebu heifer infected with *T. vivax* (Ogwu, 1983), severe inflammatory reactions of the vulva of *T. brucei*-infected rabbit (Van den Ingh and Van Djik, 1975) and swelling of the vulva in *T. evansi*-infected rabbits (Patel *et al.*, 1983).

2.3 MECHANISM OF REPRODUCTIVE DISORDERS.

The mechanism of tissue and organ damage in trypanosomosis that result in reproductive disorders are not well-understood. In the female the following have been incriminated:-

i. Pyrexia:

The observed infertility and conception failures in female animals with trypanosomosis is partially due to chronic fluctuating pyrexia caused by the infection. Pyrexia has been shown to adversely affect the uterus, ova, spermatozoa and embryo, through detrimental effects on the ovarian and tubal function(Ogwu *et al.*, 1984). Hyperthermia causes morphological abnormalities in eggs, e.g shrunken cytoplasm, ruptured vitelline membrane or zona pellucida, or may act directly by alteration of the milium interior of the uterus, thereby making it hostile to the foetus (Hafez, 1968), resulting in abortions, conception failure and embryonic death observed in animal trypanosomosis.

ii. Direct Effect of Trypanosome:

Another possibility for the conception failure, embryonic and foetal death is the direct effect of the trypanosome on the embryo, foetus and pregnant uterus. Transplacental transmission of pathogenic trypanosome and infection of the foetus in-utero have been reported (Ikede and Losos, 1972; Ogwu and Nuru, 1981; Ogwu *et al.*, 1986). For the fetus to be infected from the maternal circulation, trypanosomes must cross tissue barriers (Ogwu and Nuru, 1981). This may involve placental damage which has been demonstrated by

Ogwu (1983). He reported patho-histological lesions in the placenta of *T. vivax*-infected pregnant heifers. This will result in the invasion of the embryo by the trypanosomes and embryonic death (Ikede and Losos 1972; Isoun & Esuruso, 1972; Ogwu and Nuru, 1981; Ogwu *et al.*, 1984; 1986).

iii. Endocrine changes:

The endocrine system has frequently been investigated in ruminant trypanosomosis (Ikede and Losos, 1975; Masake, 1980;Mutayoba *et al.*,1988a; Abebe and Iley, 1992a; Ogwu *et al.*,1992). Plasma thyroxine, cortisol, and gonadotrophins have been shown generally to be reduced. These findings probably explain some of the marked effects of trypanosome infection on growth, metabolism and reproduction because of the role of hormones in such processes (Jeffcoate and Holmes, 1997). Disruption of cyclic activities and abortions caused by pathogenic trypanosome have been reported (Ogwu, 1983; Adenowo, 1989; Sekoni, 1994). This has partly been associated with depressed progesterone production and elevation of corticosteriods levels respectively (Sekoni,1994). Adenophyseal lesions reported in animal trypanosomosis (Ikede and Losos, 1975; Masake, 1980; Morrison *et al.*, 1981) have, been reported to interfere with estrous activities.

Estrous activities are controlled by an intricate balance between gonadotropic releasing hormone (Gn/RH) gonadotrophins (FSH and LH) and sex steroids (estrogen and progesterone) (Sekoni, 1994). The lesions in the adenohypophysis will invariably lead to disruption of the normal production of gonadotropic hormones and affect estrous activities.

iv. Stress:-

Abortions observed in trypanosomosis is partly due to both maternal and foetal stress factors. These include severity of the infection, pyrexia, foetal hypoxia due to

maternal anaemia, transplacental infection (Ikede and Lossos, 1972; Isoun and Esuruoso, 1972, Ogwu *et al*., 1986) and alteration of cortisol levels (Mutayoba and Gombe, 1989; Ogwu *et al*., 1992). It is suggested that the hypothalamic stress caused by trypanosomosis infection in animals leads to elevation of plasma cortisol levels, thereby resulting in abortions.

2.4 INTRA UTERINE INFECTION:

Transplacental transmission of infection is the passage of the maternal infection across the placenta itself, the consequences of such foetal infection includes foetal death, abortion, foetal malformation, persistent infection, subclinical infection of no serious consequences (Osburn and Kennedy, 1981) and premature delivery.

Reviews by Nuru (1974) and Ogwu and Nuru (1981), gave evidences of transplacental transmissions of trypanosomosis in animals and man. Termination of pregnancy in *T. vivax* infected cows was observed by Nuru (1974). A cow inoculated with blood from the aborted foetus became parasitaemic, suggestive of transplacental transmission. Ogwu *et al*.,(1986) also reported transplacental transmission of pathogenic *T. vivax* to calves, which were highly parasitaemic, anaemic or weak and with low birth weights. Pathogenic trypanosome have also been demonstrated in amniotic fluid of *T. vivax* infected pregnant sheep (Isoun and Anosa, 1974) and in lambs (Ikede and Losos, 1972)). Elhassan (1987), also demonstrated infection of *T. vivax* in two aborted foetuses from ewes experimentally infected, in the first trimester and in a lamb born at term from a ewe that was infected in the third trimester of pregnancy.

The mechanism(s) by which trypanosome pass the placenta barrier is not fully understood. Placental damage may be necessary for the trypanosome to cross this barrier (Sekoni 1994). Ogwu (1983), demonstrated damages to placenta in *T. vivax* infected

pregnant heifers. He observed histological lesions in the placenta of the infected heifers. Trypanosome have also been known to possess biologically active substances such as enzymes:- protease, phospholipase and vascular permeability factors (Tizard *et al*., 1978a). These enzymes may act together with other proteases on a number of biologically significant substrates such as plasminogen and fibrinogen (Borehan and Facer, 1973). Phospholipase are capable of destroying cell membrane phospholipids, thereby facilitating the passage of trypanosome and infection of the foetus.

2.5 IMMUNITY IN TRYPANOSOMOSIS

The typical primary immune response of mammals in which IgM synthesis is replaced by the synthesis of IgG antibodies is modified in trypanosome infected hosts in that IgM production is greatly enhanced and prolonged (Vickerman and Barry, 1982). Elevated serum IgM of up to 9-folds have been reported in natural and experimental infections of bovine with *T. brucei*, *T. vivax* and *T. congolense* (Hudson *et al*., 1976; Luckins, 1976). IgG levels have been shown to change up to 2-folds in cattle experimentally infected with *T. congolense* or *T. vivax*. Similar increases of IgG of up to 2-folds have also been recorded in natural infections of trypanosomosis in cattle and bush-buck (Luckins,1975; 1976). IgM is reported to be more effective than early IgG at neutralizing, agglutinating and lysing trypanosome in-vitro and providing protection in-vivo (Seed, 1972; Takayanagi and Enriquez, 1973; Luckins, 1976; Musoke *et al*., 1981). Variable antigen type(VAT) specific antibody is reported present in both IgM and IgG fractions.

Destruction of trypanosome is antibodies-mediated; studies have shown that VAT-specific antibodies bind to trypanosome readily and cause various detrimental effects including agglutination (Cunningham and Vickerman, 1962) decreased respiratory rate

(Desowitz, 1959; Thurston, 1958) and uptake of Leucine (Diggs *et al.*, 1976)and lysis of trypanosomes (Lourie and O'Connor, 1936; VanMeirvenne *et al.*, 1975). In-vivo antibodies effect the removal of circulating trypanosome by trypanolysis and opsonization, followed by Kupffer cells uptake of the trypanosomes. Extra vascularly, various macrophages and lysis will be expected to effect removal. (Vickerman and Barry, 1982). The existence of both specific and non-specific immunity to trypanosomiasis has been shown in game animals (Hawking *et al.*,1973; Rickman, 1981).

2.5 TRYPANOTOLERANCE

Trypanotolerance refers to "reduced susceptibility" of animals to trypanosomosis. Evidence suggests that tolerance results from a complex mixture of innate, non-specific and specific acquired immune mechanisms mediated by physiological biochemical and immunological factors (Vickerman and Barry, 1982).

Different breeds of cattle, sheep and goats differ in degree of susceptibility (Coulomb *et al.*, 1978; Griffin and Allonby, 1979a,b,c). Tolerance is heritable and is intermediate in cross bred. Cross breeding experiments have shown that tolerance is inherited as a dominant trait (Morrison and Murray, 1979a). Several observations have implicated specific immune mechanism in cattle trypanotolerance, a correlation between lytic antibodies levels and tolerance have been observed. Tolerant Ndama cattle have been shown to consistently display high serum antibody levels, whereas elevated antibody levels in susceptible Zebu cattle tend to follow parasitaemia peaks (Desowitz, 1959; Luckins, 1976). A major requirement for development and maintenance of the trait of tolerance is that the host must be subjected to constant challenge from trypanosome-infected flies. Antibody response to trypanosomosis in normally tolerant breeds, raised in tsetse free

conditions have been shown to be much reduced and to resemble those of susceptible cattle (Dosowitz, 1959).

Resistance to trypanosomosis is determined by at least 3 main factors viz-ability to develop effective immune response, ability to control parasitemia and ability to resist anaemia(Murray,1988). If response by specific immunity is rapid and maintained at high level, the life expectancy of the host is greater. Tolerant Ndama cattle have been shown to consistently display high serum antibody levels, whereas elevated antibody levels in susceptible Zebu cattle tend to follow parasitaemia peaks (Desowitz, 1959; Luckins, 1976).

Severity of anemia in cattle is reported related to intensity and duration of parasitaemia (Esievo *et al.*, 1982). The concentration of sialic acid in cattle is reported to influence the degree of anaemia observed in infected cattle(Murray *et al.*,1977a), hence their tolerance to trypanosomosis. Shugaba *et al.*,(1994) reported a much higher concentration of O-acetylated sialic acids in Ndama cattle than Zebu cattle. O-acetylated sialic acids are reported to generally resist rapid hydrolysis by sialidases (Schaver *et al.*,1974; Veh *et al.*,1979). The finding of a much higher O-acetylated erythrocyte sialic acid in trypanotolerant Ndama cattle support the observation of Murray *et al.*, (1977a), that Ndama require a much higher trypanosome parasitaemia to produce the same degree of anemia with Zebu cattle. Ndama cattle possibly achieve their tolerance in part through a reduced rate of release of erythrocyte surface sialic acid by trypanosomes sialidase due to the occurrence of higher concentration of O-acetyl groups in their sialic acids(Shugaba *et al.*,1994).

Other factors of physiological and metabolic nature such as heritable differences in blood groups, thermoregulatory ability, sweat evaporation rates, metabolic efficiency are possibly involved in trypanotolerance (Coulomb *et al.*, 1978), though direct link with

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decreased susceptibility has not been established for any of these. Non heritable factors such as nutritional status and intercurrent infections also have influence.

2.6 IMMUNOSUPPRESION

Immunosuppression is an important feature of the pathology of African trypanosomosis. In some cases it is only evident during the terminal stages of infection. Immunosuppression is most marked in cases with high parasitemia and least in cases with low parasitaemia (Vickerman and Barry, 1982). Immuno-suppression renders the host more susceptible to secondary infections or show diminishing response to viral and bacterial vaccines (Vickerman and Barry, 1982). Treatment of the trypanosome infection restores immunocompetence and enables the host to mount a full secondary response(Wellhausen and Mansfield, 1980; Duncan *et al.*, 1990). Cell-mediated response may also be depressed by trypanosome infection. The depression can be abolished by drug treatment.

2.7 IMMUNOPATHOLOGY

Outstanding pathological effects of African trypanosome infections are anaemia, tissue lesions, lymphoid cells proliferation, circulatory disturbances associated with increased vascular permeability and imunodepression (Murray, 1979). Vascular disturbances and disruption of tissue architecture (more importantly in heart and brain) are common in both human and animal trypanosomosis (Vickerman and Barry, 1982).

Goodwin (1974), reported that antigen-antibody reactions in trypanosome infection cause the release of kinins, histamines and other pharmacologically active substances, resulting in increased vascular permeability, swollen blood vessels etc. The resultant Oedema and extra vasation of parasites and leucocytes may among other effects, cause the separation of myocardial fibers. This might affect the conduction of impulses within the heart. Blindness may also result from too much pressure due to fluid accumulation in the

chambers of the eye (Ikede and Losos, 1975). Damage to blood vessels may lead to fibrinous exudation into organs as the lungs as has been observed in *T. vivax* infected animals (Masake, 1980; Anosa, 1983).

Deposition of immune-complexes has been reported by Murray (1974) and Nagle *et al.*,(1974) and associated with renal insufficiency in *T. brucei* infected rabbits (Goodwin and Guy, 1973). Morrisson *et al.*,(1978) reported that the phagocytosis of immune complexes by macrophages leads to the leakage of enzymes from the macrophages into the surrounding tissues which may be cytolytic to the tissue cells.

2.8 THE PARASITE

The African salvarian Trypanosome as a free swimming parasite, found in the blood stream of the mammalian host, is made up of a kinetoplast, nucleus, a plasma membrane and a flagellum. It has a surface coat which is a layer of glycoprotein, which envelopes the whole plasma membrane of the parasite body and flagellum. The coat serves as a protective clothing which enables the trypanosome to establish itself in the host in the face of non-specific defense mechanism, and specific (lymphocyte-mediated) defence mechanisms, which come into play later. This is possible because the trypanosome is able to change the antigenic nature of glycoprotein which composes the coat so that the host's acquired immune response is in-effectual, and response to the new antigen is called for. It is this **antigenic variation** - the tireless repetition by the trypanosome population of such changes of coat, which may lead to the host literally destroying itself in its vain attempt to overcome the infection (Vickerman and Barry, 1982).

African trypanosome contain two functional groups of antigens: Common (stable) antigen's and variable antigens. Common antigens are components of the plasma membranes and organelles and can be isolated from the trypanosome population at any

point in its infection of the mammal. They are also the same in all trypanosome in an infection and at all stages of an infection (Vickerman and Barry, 1982). The same antigens may be found in other stocks of the same species, some in other species and some persist throughout the life cycle of the trypanosome (Le-Ray, 1975).

Variable antigen, completely cover the surface of the plasma membrane of a trypanosome. They change from one population of trypanosome to another and are responsible for differences between serological variants or variable antigen types (VAT'S) of the trypanosome (Vickerman and Barry, 1982). An individual trypanosome expresses only one variable antigen type. In the absence of a surface coat trypanosome cannot survive in the mammal. They are killed by non-specific immune responses. The surface coat variable surface glycoprotein (VSG) is highly immunogenic and stimulates strong specific antibody dependent immunity.

Antigenic variation occurs in infection initiated by a single trypanosome (Ritz, 1916). This term denotes the process of switching from expression of one variable antigen type to that of another. Switching occurs spontaneously in a process that does not require the presence of antibody as a stimulus.

During the course of an infection with any of the three pathogenic species of trypanosome, parasitaemia fluctuates dramatically (Vickerman and Barry, 1982). These fluctuations are caused by the interaction of growing trypanosome populations undergoing antigenic variation, with VAT- specific immune responses. In a relapsing parasitaemia, the different peaks of trypanosome population belong to different VATs (Capbern *et al.*, 1977).

In the first peak of parasitaemia following cyclical transmission, the M-VAT's are first to be detected, followed by the characteristic predominant VAT's which may depend

on the VAT ingested by the infecting fly (Gray, 1965). Each parasitaemic wave consists of many sub-populations of trypanosomes, each expressing a different VAT. Some of these sub-populations are larger than others. As protective immune responses kill trypanosome expressing the most common VAT, the parasitaemia goes into remission until trypanosome sub-populations expressing rarer VATs grow to cause a further relapse.

In syringe passage trypanosome, one VAT, the homotype, constitutes greater than 99 percent of the population. The population also contains very small populations of other VATs *termed heterotypes.*

2.9 EPIDEMIOLOGY

Briefly, the epidemiology of African trypanosomosis is as follows:-The pathogenic animal trypanosome are transmitted cyclically, mechanically or by coitus (Anosa, 1983; Roeder *et al.,* 1984). The cyclical method which involves the bite of the vector, tsetse flies (Glossina) found in sub-Saharan Africa, is the most common means of infection. Trypanosome multiply within the vector to produce the infective metacyclic forms. Other biting flies such as Tabanids can transmit the parasite mechanically (Morrison *et. al.,* 1981).

The diseases caused in animals are collectively called Nagana, while in human beings they are referred to as sleeping sickness (Apted, 1970). The trypanosome develop in a cycle which involves wild animals and tsetse flies (Abou-Ela *et al.,* 1987; Ashcroft, 1959; Djabakou *et al.,* 1981; Kupper *et al.,* 1983).

Wild life animals are usually symptomless carriers of the pathogenic trypanosome. The tsetse flies become infective to animals and humans for the duration of the insect's life cycle once it has fed on carrier game animal.

2.10 THE DISEASE: AFRICAN TRYPANOSOMOSIS.

African trypanosomosis occurs across more than a third of Africa. It is arguably the most important livestock disease on the continent (ILRAD, 1990). Like East coast fever, trypanosomosis is caused by a protozoan parasite the trypanosome. The most important trypanosomes that cause disease in livestock are *T. vivax*, *T. congolense* and *T. brucei* (Ikede, 1981). In pigs, *T. simiae* is the most virulent (Leach, *et al.*, 1965). *T. vivax* is considered to be the most pathogenic and important trypanosome of ruminants (Glover, 1961; Leach, *et al.*, 1965; Agu, 1983) in West Africa, while in East Africa it is *T. congolense* (Griffin, 1978; Mwambu, 1983). *T. evansi* and *T. equiperdum* infect mainly camels and horses respectively and of economic importance in North Africa. Both are non cyclically transmitted by biting flies other than Glossina (Scot, 1973).

The disease in animals may be hyper-acute, in which case the animal dies within few hours (e.g. *T. simiae* infection in pigs); or may be acute, subacute or chronic. In the chronic form, the animal is usually emaciated, anaemic with low total plasma protein and intermittent pyrexia (Akol and Murray, 1981; Apted, 1970; Boch, *et al.*, 1984).

2.11. Pathogenesis of African Trypanosomosis:

Infection of the host begins with the injection or penetration of metacyclic forms of trypanosome into the subcutaneous or submucosal tissue. At the site of bite or injection, multiplication occurs resulting in a local inflammatory reaction "the chancre". Trypanosome from the chancre enter the blood, either through the lymphatics or directly and are disseminated throughout the body by the circulating blood leading to parasitaemia. The level of parasitaemia is a reflection of the virulence of the organism (Losos, 1986).

Anosa (1983, 1988) reported the course of the disease to be variable in both

severity and duration and also described the course of the disease to be in three recognizable phases-viz:-

Phase I Acute crisis: The acute crisis is the phase whereby the host is yet to adequately organize its defense mechanism against the parasite, thus it often succumbs to the infection unless the virulence of the parasite is not intense. It begins with the first appearance of trypanosome in blood after the incubation period. Parasitaemia is high, although with fluctuations. In acute cases, the infection is also characterized by rapidly developing pancytopenia and marked alteration in blood chemistry. The animal survives for several weeks. Death occurs because of the severe pancytopenia and other deleterious changes.

In peracute cases the parasitaemia persists without abatement. Animals die within a week of infection with *T. vivax*, *T. brucei* and *T. congolense*. Animals destined to suffer chronic trypanosomosis also manifest an acute crisis but show less severe parasitemia and pathology than animals with peracute or acute infection.

Phase 11 Chronic Crisis: This follows imperceptibly after the "acute crisis" and is characterized by low frequency and intensity of parasitaemia. It appears to be a period when the infected animal has fully mobilized its defense mechanism to a level that is adequate to completely abort the infection or reverse the pathology that developed during phase 1. Death occurs at this stage either as a result of the progressive pathology caused by the parasite per-se and/or due to secondary infections, since individuals are imunodepressed.

Phase 111 Recovery or "Post-crisis": It is characterized by low very infrequent parasitaemia, symbolizing the capitulation of the parasite to the host's defense mechanism. The leucocyte, erythrocyte and thrombocyte levels begin to recover towards pre-infection levels, albeit slowly and other pathological changes are slowly reversed. The pathogenesis of trypanosomosis, have been based on three main factors namely, anaemia, tissue lesions,

and imuno-depression(Urquhart,1980).

2.11.Anaemia:

Anaemia is a consistent finding in various trypanosome infections(Saror, 1980; Anosa, 1988). The anaemia of trypanosomosis usually set in during the first wave of parasitaemia and its subsequent development is determined by the frequency and intensity of the parasitaemia (Anosa, 1988). Several mechanisms have been implicated in the anaemia of trypanosomosis infections and these include haemolysis, dyshaemopoiesis, haemodilution and haemorrhage (Anosa, 1988).

2.11.1. HAEMOLYSIS- The aetiology of the haemolysis is complex, involving many factors which are related directly or indirectly. These are: Immunologic mechanisms, haemolytic factors, disseminate intravascular coagulation, mononuclear phagocytic system, fever and direct trauma to the erythrocytes.

i.Immunologic mechanisms

Restriction of parasite growth is primarily mediated by immunological mechanism. Rats infected with *T. evansi*, showed significant immune responses to the infecting trypanosomes. With peak agglutinin titres occurring 10-12 days pi, coinciding with period of maximum destruction of erythrocytes (Assoku, 1975). Further evidence supporting the immunological basis of anaemia in animal trypanosomosis is the elevation of IgM (Clarkson, 1968; Clarkson *et al.*, 1975; Kobayashi and Tizard 1976; Luckins and Mehlitz 1978) and complement fragments on cell surfaces, during the disease (Kobayoshi *et al.*, 1976; Amole *et al.*,1982; Facer *et al.*, 1982). These complexes attach to erythrocytes membranes and render them more susceptible to phagocytosis by macrophages.

Anosa (1988), postulated that erythrocytes haemolysis is caused by the erythrocytes acquiring antigens released by live trypanosome or following trypanolysis or adhesions of

the trypanosome to the erythrocytes leading to coating of the erythrocytes with anti-trypanosome antibodies (IgM and IgG), thereby rendering the erythrocytes susceptible to phagocytosis. Preformed Trypanosoma antigen-antibody complexes may also attach to the erythrocytes leading to phagocytosis.

Several reports consider these immune mechanisms to be important causes of anaemia, particularly in the early phase of the infection, based on observations that IgM binding to erythrocytes was marked in the acute phase of the infection, but no longer demonstrated in the chronic stage when parasitaemia was low and erythrocytes values have improved slightly (Anosa, 1988).

ii. Haemolytic factor

The existence of haemolytic factors was first suggested by Fiennes (1954), who observed that red cells from nomal bovine blood were haemolysed when incubated with plasma from trypanosome infected animals. The production of haemolytic factors have been reported to coincide with major haemolytic changes during the course of experimental *T. brucei* infection in mice (Nguyen Huan *et al*., 1975). This factor has also been found to be produced by other typanosomes such as *T. vivax* infection in cattle, but its role in the development of anaemia was not ascertained (Murray *et al*., 1977b). This haemolytic factors might be phospholipase, fatty acids (Tizard *et al*., 1978b).

Proteins from trypanosomes, of molecular weight 10,000 daltons are reported capable of lysing erythrocytes(Huan *et al*.,1975). Haemolysin secreted by live trypanosome or released following trypanolysis have also been shown to cause hemolysis in-vitro and may play a role in in-vivo hemolysis(Tizard *et al*., 1978a).

iii. Disseminated Intra Vascular Coagulation

Widespread occurrence of fibrin deposits in the microvasculature of various body

organs of trypanosome infected sheep and goats has been reported (Anosa and Isoun, 1983). These have been shown to distort the shape of erythrocytes (schistocyte), which are then rendered liable to lysis or phagocytosis (Wintrobe, 1975). This may account for the observations of marked alterations in erythrocytes morphology, including erythrocyte fragments in *T. brucei* - infected rabbits and cattle infected with *T. congolense* (Valli *et al.*, 1979; Jenkins *et al.*, 1980). Erythrocyte fragmentation may lead to microthrombi, vascular damage, splenomegaly or glomerulonephritis, resulting in the production of schistocyte, microspherocytes and spherocyte which are phagocytized and inducing micro-angiopathic haemolytic anaemia (Anosa, 1988).

iv. <u>Mononuclear Phagocytic System (MPS)</u>

Animal trypanosomosis have been reported to be characterized by expanded and active MPS, which develops soon after infection and continues throughout the disease (Murray, 1974). This is manifested by lymphadenopathy and splenomegaly (Fiennes, 1970; Anosa and Isoun, 1983). Splenomegaly may result in erythrocyte stasis causing prolonged contact with the expanded and active MPS, hence increase lysis and erythrophagocytosis(Murray, 1979). The demonstration of erythrophagocytosis and haemosiderosis in the spleen of animals infected with *T. vivax* (Van den Ingh *et al.*, 1976; Anosa and Isoun, 1983) lends credence to this postulation.

The phenomenon of erythrophagocytosis is well documented as contributing to the anaemia of trypanosomosis in rabbits (Boycott and Price Jones 1913); sheep (Mackenzie and Cruikshank, 1973), goats (Saror, 1980), and cattle (Fiennes 1954; Naylor 1971a; Losos *et al.*, 1973). Trypanosome antigens attach to the surface of red cells, leading to their subsequent combination with anti-trypanosome antibodies in plasma and the eventual sequestration of the red cells by erythrophagocytosis(Jennings, 1976).

The production of sialidase by *T. vivax* (Esievo, 1979) and the cleavage of erythrocyte surface sialic acid during bovine trypanosomosis (Esievo, 1980), present new antigenic sites on the affected erythrocytes (Pirofsky, 1969). Antibody is reported to be produced against these new antigenic sites on the erythrocytes to render them suitably for erythrophagocytosis (Esievo and Saror, 1991).

v. Fever- Fever, a consistent finding in trypanosome infection has been suggested as possibly inducing erythrocyte damage and phagocytosis based on studies on its effects on erythrocytes (Anosa, 1988).

vi. Direct trauma to erythrocytes

The lashing action of trypanosome may inflict injuries on erythrocytes when parasitaemia is high (Wintrobe, 1975). Anosa and Kaneko (1983) and Anosa (1988) suggested that, the many tiny foci of discontinuity made on the surface of erythrocytes membranes at the points of contact between trypanosome and erythrocytes render the cells more susceptible to phagocytosis by macrophages.

vii.Reduced lifespan of erythrocytes.

Mamo and Holmes (1975), suggested that the lifespan of erythrocytes is reduced during the acute-phase of trypanosomosis. Esievo (1980), demonstrated increased production of neuraminidase in cattle infected with *T. vivax* and suggested that this enzyme cleaves sialic acid from erythrocytes surface, which render them more susceptible to phagocytosis and that significant reduction in erythrocyte sialic acid reduces the lifespan of erythrocytes.

2.11.2.DYSHAEMOPOIESIS

Depressed erythropoiesis and degenerative changes in the marrow have been reported in trypanosomosis of rabbit and cattle(Boycott and Prince-Jones, 1913; Fiennes,

1954; Losos and Ikede, 1972). In other studies active erythropoiesis have been reported in sheep, goat and cattle (Mackenzie and Cruikshank, 1973; Saror, 1980 and Ingh *et al.*, 1967).

Microcytosis (Fiennes, 1970); hypoferremia (Tautor and Idris, 1973) and plasma iron turnover rates(Dargie *et al.*, 1979b) observed during chronic trypanosomosis have been reported as suggestive of impaired erythropoiesis. This finding coupled with the build-up of hemosiderin deposits (Saror, 1980; Anosa and Isoun, 1983) suggests defective iron utilization and raises the possibility that in long standing infections, the marrow is effectively starved of iron and anaemia may be complicated by dyshaemopoiesis.

2.11.3.HAEMODILUTION

Haemodilution has been suggested by many authors as contributing to the pathogenesis of anaemia. Naylor (1971), described a 30% increase in the plasma volume of cattle infected with *T. congolense*. Likewise, Anosa and Isoun (1976), concluded that hypervolaemia associated with increased plasma and reduced red cell volume was a feature of *T. vivax* infections in sheep and goats. There has been no satisfactory explanation as to the exact mechanism of haemodilution, and as such, its role has been questioned by several workers(Jennings *et al.*, 1974; Dargie, 1978; Maxie and Valli, 1978; Dargie *et al.*, 1979b).

However, haemodilution could contribute meaningfully to the pathogenesis of anaemia only if the plasma volume increases out of tune with the attendant drop in erythrocyte volume(Maxie and Valli, 1978). Anosa (1988), reported increase in plasma volume as a consistent finding in trypanosome anaemia, and that the increase is a pathophysiological compensation mechanism to maintain total blood volume. Dargie *et al.*,(1979a), reported that haemodilution is not a feature of animal trypanosomosis.

2.11.4. HAEMORRHAGES

Haemorrhages have been reported in acute *T. vivax* infection of cattle sheep and goats. However, these haemorrhages were minor and most likely do not contribute significantly to the anaemia(Anosa, 1988).

3.0 CHAPTER THREE

CLINICAL MANIFESTATIONS OF *Trypanosoma vivax* INFECTION IN YANKASA AND WEST AFRICAN DWARF (WAD) EWES IN THEIR FIRST, SECOND AND THIRD TRIMESTERS OF PREGNANCY.

3.1 SUMMARY

Three groups of ewes made up of six pregnant Yankasa and six pregnant WAD ews in each group, were assigned at random to first, second and third trimester of pregnancy to study the clinical manifestation of *T. vivax* infection. The ewes became parasitaemic 3-4 days after infection. The severity of the infection in the Yankasa ewes increased as the pregnancy advanced in the ewes. The infection was most severe in Yankasa ewes in the third trimester and WAD ewes in the second trimester. Yankasa and WAD ewes in the first trimester were least susceptible to the infection. Self cure from the infection was observed in one of the WAD ewes infected in the first trimester.

Anaemia was observed in the infected Yankasa and WAD ewes in three trimesters of pregnancy. Loss in body weights were observed in the infected Yankasa in all the trimesters of pregnancy, but observed in the WAD ewes in the second and third trimesters of pregnancy. Infected WAD ewes in the first trimester showed increase in body weights. Abortions were observed in the Yankasa ewes in all the trimesters, but observed in the WAD ewes in the second and third trimesters only. The WAD ewes tolerated the effects of the infection on anemia, body weights and pregnancy better than the Yankasa.

It was concluded from the study that the clinical manifestation of *T. vivax* infection in pregnant Yankasa and WAD ewes was influnced by stage of pregnancy and breed ewes.

3.2 INTRODUCTION

Animal trypanosomosis caused by *Trypanosoma vivax, T. brucei, T. congolense* is one of the most important diseases of livestock in West Africa. *T. vivax* is regarded as the predominant cause of bovine trypanosomosis in Nigeria (Leeflang, 1975) and probably the most pathogenic (Ikede, 1982). Trypanosomosis is partially responsible for nomadism, transhumance and their attendant socio-economic problems in Nigeria (Asuamah, 1977). Trypanosomosis is also responsible for restricting some breeds of livestock especially cattle, sheep and goats to the Sahel and Northern Sudan vegetation zones, where rainfall and pastures are limited and for rendering the lush pastures of the South not available for grazing.

The Zebu breed of cattle which are predominantly found in the Sahel and Northern Sudan vegetation zone, have been regarded as susceptible to trypanosomosis (Desowitz, 1959). These breeds of cattle can be subjected to fatal infections particularly in areas of heavy challenge. They can however survive in areas where the challenge is low and grazing conditions are good (Desowitz, 1959). In contrast, the breeds designated by Stewart (1951), as the West African short horn (Ndama and Muturu) distributed in the Guinea Savannah and Forest zones of Nigeria, possess considerable tolerance to trypanosomosis (Chandler, 1952) and can survive in areas where the challenge is heavy.

Small ruminants (Sheep and goats) indigenous to Nigeria, are likewise restricted in their habitation of the various ecological zones of Nigeria by trypanosomosis. Trypano-susceptible breeds of sheep, Yankasa and Balami in Nigeria (Edeghere *et al.*, 1986; Adenowo, 1989; Bawa *et al.*, 1990; Maikaje *et al.*, 1991) are found in the Sahel and Sudan Savannah, where tsetse and trypanosomosis challenge is light or absent. In contrast the

breeds referred to as tolerant to trypanosomosis (Griffin and Allonby 1979 a,b,c; Toure *et al*., 1981), thrive very well in ecological zones such as the Guinea Savannah, and Forest zones of Nigeria where tsetse and trypanosomiasis challenge are heavy.

The susceptibility/tolerance of these breeds of livestock is influenced by several factors such as:- Immunologic response of the host to the infection (Desowitz, 1959; Luckins, 1976), transfer of maternal antibody from dam to offspring and constant exposure to the parasite in endemic areas. Others are inter current diseases, nutrition, stress of migration and pregnancy, management (Stewart, 1951; Desowitz, 1959; Godfery *et al*.,1964; Stephen, 1966; Touchberry, 1967; Mortelmans and Kageruka, 1976; Ogwu, 1983). Lactation, level of tsetse challenge, sex, age (ILCA, 1984); haemoglobin type (Bangham and Blumberg, 1958)and genetics (Roberts and Gray, 1973) are also contributory to the tolerance or susceptibility of livestock to trypanosomosis. The high concentration of O-acetylated sialic acids in the erythrocytes of Ndama cattle is also reported to influence their tolerance to trypanosomosis (Shugaba *et al*., 1994).

The pathogenesis of trypanosome species infection in animals is reported to be similar. The most characteristic feature is the development of anaemia(Morrisson *et al*., 1981; Anosa, 1988). Anaemia has long been established as a significant pathological feature of animal trypanosomosis. Death of dams during pregnancy or shortly after parturition of usually weak/dead offsprings or expulsion of abnormal or dead foetuses (Ogwu, 1983; Sekoni, 1994) has also been associated with trypanosomosis.

The clinical manifestations of *T. vivax* infection on Uda rams and Yankasa ewes (Adenowo, 1989; Maikaje *et al*., 1991) have been reported. Similarly preliminary studies on the effects of *T. vivax* infection on second and third trimester of pregnant Yankasa and WAD ewes have also been reported (Bawa *et al*., 1990). The effects of pregnancy on

clinical manifestations of trypanosomosis in Zebu cattle have been described (Ogwu and Njoku, 1987). Comparative studies on the clinical manifestation of *T. vivax* infection on pregnant Yankasa and WAD ewes in Nigeria is lacking. This study was therefore designed to study the clinical manifestation of *T. vivax* infection on pregnant Yankasa and West African Dwarf sheep infected in the first, second and third trimesters of pregnancy.

3.3 MATERIALS AND METHODS

Animals and Experimental Design.

Seventy five (75) normocyclic ewes made up of forty five (45) Yankasa and thirty (30) West African Dwarf (WAD) ewes, with average weights of 29.8 ± 2.1kg and 21.0 ± 1.3kg respectively, were acquired for the study. The Yankasa ewes were acquired from the tsetse-free Sudan savanna zones of Nigeria (Kaduna and Katsina States), while the WAD ewes were acquired from the tsetse-infested Forest zone of Nigeria (Edo State). Before the commencement of the study, the WAD ewes were allowed to acclimatize for six months. Baseline hematological data, progesterone(P4) values and cyclicity of the ewes using vasectomized rams and P4 determination were evaluated, during the period of acclimatization. The ewes (Yankasa and WAD)were also checked for blood and intestinal parasites at monthly intervals during this period. They were grazed on improved pastures and supplemented daily with a concentrate mixture of 60% maize and 40% cotton seed cake. The ewes were fed 300.0 gms of the concentrate mixture per ewe per day.

They were deticked at two weekly intervals, using the acaricide, Rhodiacide (Rhone-Poulene Agrochime, Germany) and dewormed before the commencement of the study using flukazole (Chanelle - Ireland England). The presence of trypanosome and other

haemoparasites in the ewes were investigated using the haematocrit centrifuge technique (Woo, 1969) and the thin blood smear method.

To get the ewes in the same phase of reproduction, they were synchronized for estrus using intravaginal sheep sponges (Veramix^{R}, Up John Ltd, U.K.), containing 60.0mg of Medroxy-progesterone acetate as active ingredient. The sponges were removed at thirteen (13) days post insertion and intact proven fertile Yankasa and WAD rams at a ratio of 1 ram to 5 ewes, were introduced to breed the Yankasa and WAD ewes respectively, forty eight (48) hours after sponge withdrawal. Pregnancy was diagnosed in the ewes by Radio- immunoassay technique of progesterone determination.

Progesterone Assay:

Progesterone values of the ewes sera samples were determined using the solid phase radioimmunoassay technique for progesterone determination, as described by Pathiraja *et al*.,(1986); Oyedipe *et al*.,(1986). Progesterone concentration of the samples were determined using FAO/IAEA progesterone RIA kits, supplied by the Animal Production and Health Unit. FAO/IAEA Laboratories, International Atomic Energy Agency Seibersdorf, Vienna Austria. Tubes coated with monoclonal antibodies against 11-alpha-hemisuccinate progesterone-BSA, were titrated with serum progesterone standards (0.0 to 63.6nm/L), internal and external progesterone quality control samples and serum samples from the ewes, in 100ul volumes. Radioactive tracer- Progesterone 11-alpha-hemisuccinate-2-[^{125}I] iodohistamine solution, was then added to the coated tubes with the test sera samples, standards and quality control samples in 1000uL volumes. The mixture was vortexed and incubated for 3 hours at room temperature. Thereafter, the unbound tracer to the antibody coated tubes and the unbound progesterone in the test sera samples, standards and quality control samples was decanted. The amount of the tracer or

progesterone in samples/ standards bound to the antibody coated tubes was determined on a Nuclear Enterprises Gamma counter NE 1612 Nuclear Enterprises. The amount of the tracer bound to the antibody coated tubes, was inversely proportional to the amount of the progesterone in the sample or standard, bound to the antibody coated tubes. The standards provided have been validated to cover the physiological progesterone concentration range prevalent in the blood serum or plasma of most domestic livestock species. The concentrations of the progesterone in the samples were determine from the log-git graph plotted from the percentage binding of the standards(B/BO) Versus the progesterone concentration of the standards. The B-maximum values of all the assays ranged between 47% to 56%. Measure of the variation of samples i.e precision and reliability of the assay procedures were taken into account. The intra-assay and inter-assay coefficients of variations of the assays were 6.0-7.8% and 9.4-10.0% respectively. Ewes with progesterone values greater than 1.0ng/ml by 18 days post breeding and did not return to oestrus by 21 days post breeding were considered pregnant.

Forty two(42) of the ewes confirmed pregnant, made up of 21 Yankasa and 21 WAD were selected for the study. The ewes were paired according to body weights and assigned to three groups of 6 pregnant Yankasa and three groups of 6 pregnant WAD ewes at random, for first, second and third trimester studies. A fourth group made up of 3 pregnant Yankasa and 3 pregnant WAD ewes formed the controls.

INFECTION:-

Stabilates of *Trypanosoma vivax* (Stabilate 150), were obtained from the Department of Veterinary Parasitology and Entomology Faculty of Veterinary Medicine, Ahmadu Bello University Zaria, for infection from donor goats. Blood from the donor goats was used for infecting the experimental ewes at each stage of pregnancy. This strain of *T. vivax* was first

isolated from a bovine at Kaya Village in Zaria. It was cloned and pasaged twice in goats before it was cryo-preserved in DMSO and kept in liquid nitrogen as Stabilate 150.

The ewes in the first, second and third trimesters of pregnancy were each infected by jugular veni-puncture at 23, 52 and 106 days of pregnancy respectively, with 2.0mL of blood from a donor goat containing 2×10^6 trypanosome. The ewes in the control group were left un-infected(hence controls).

Following infection the ewes were monitored for daily clinical signs, rectal temperatures and parasitaemia. Packed cells volume(PCV) and serum samples for progesterone determination were taken twice weekly. Body weights were determined weekly. Blood samples for determination of parasitaemia and PCV, were taken between 8-10.0am in test tubes containing 10% ethylene diaminetetracetate (EDTA), as anticoagulant. One test tube was used for each animal.

Parasitaemia in the ewes was determined within 30 minutes of collection. The microhaematocrit centrifuge technique(HCT) was used. The parasitemia was determined by examination of the buffy coat plasma junction of the capillary tube of each sample. The degree of parasitaemia was classified according Woo, (1969) as follows:-[1]+, occasional trypanosomes seen; [2]++, 1-2 trypanosomes seen; [3]+++, 3-20 trypanosomes seen; [4]++++, greater than 20 trypanosomes seen per buffy coat area.

The PCV of the samples were determined after the determination of the parasitaemia of the samples. The PCV of each sample was read from the sample's HCT capillary tube, using a Gelman Hawskley microhematocrit reader (Gelman. Hawksley Ltd. England) and recorded as percent.

Rectal temperatures of the ewes were taken between 8.00 - 10.00am using a centigrade thermometer. Body weights were determine in the morning before feeding the

animals. A top loading scale model D, was used for the determination of body weights and recorded in kilograms (kg). Percentage changes in body weights post infection were calculated and recorded for the ewes.

STATISTICAL ANALYSIS:-

Statistical analysis of the data was done as described by Steel and Torrie (1980), using SAS package. Treatment groups comparison was done using Duncan treatment comparison method.

3.4 RESULTS

Tables 3.1 and 3.2 are tabulations of the clinical manifestations and haematological values of the Yankasa and WAD ewes respectively. The statistical analysis of the clinical data of the ewes are shown in Appendix 1.

FIRST TRIMESTER

Clinical Signs:

In the first trimester group, the clinical manifestation of the infection was mild in both the Yankasa and WAD ewes and was characterized by raised hair coats, enlarged prescapular lymph nodes, fluctuating parasitaemia and pyrexia, minimal lost in body weights in the Yankasa ewes. Apart from these observations, both the Yankasa and WAD ewes in the first trimester group were apparently normal, alert, active and with good appetite.

Table 3.1: CLINICAL OBSERVATIONS ON YANKASA EWES INFECTED IN THEIR FIRST, SECOND AND THIRD TRIMESTERS OF PREGNANCY.

GROUPS OF EWES Pregnancy stages	YANKASA FIRST	SECOND	THIRD	CONTROLS
Nature of infection:-	Mild	Severe	V.Severe	Nil
Death of Dam	Yes	Yes	Yes	Nil
Abortions	No	Yes	Yes	Nil
Foetal resorption	Yes(1)	Yes(1)	No	Nil
Dystocia	No	No	No	Nil
Lambing	No	No	No	Yes
Parasitaemia Range	0-4	0-4	0-4	Nil
Mean±SD	3.4±3.7	2.9±1.1	2.3±1.2	Nil
Rectal Temperature Range:-0C	36.8-41.5	38.1-41.3	38.3-40.9	38.2-39.2
Mean±SD-0C	39.6±1.2	39.2±0.8	39.2±0.7	38.7±0.3
Highest Value pi.0C	41.5	41.3	40.9	-
%PCV Values Range	15.0-29.0	11.0-30.0	10.0-31.6	26.0-36.0
Mean±SD	21.3±3.6	22.2±4.3	19.9±6.8	29.0±3.0
Lowest Value pi	15.0	11.0	10.0	-
Plasma Proteins Values(g/dL) Range-	5.6-8.3	5.3-9.1	5.0-8.3	6.2-9.0
Mean±SD	6.3±0.8	6.7±0.9	6.5±0.8	7.4±0.4
Lowest value pi	5.6	5.3	5.0	-
Highest %Change in body weight	-8.31	-23.0	-35.5	+6.8

KEY (-) Loss in body weights of ewes.
(+) Increase in body weights of ewes.

Table 3.2: CLINICAL OBSERVATIONS ON WAD EWES INFECTED IN THEIR FIRST,SECOND AND THIRD TRIMESTERS OF PREGNANCY.

GROUPS OF EWES	W A D			
Pregnancy stages	**FIRST**	**SECOND**	**THIRD**	**CONTROLS**
Nature of infection:-	Mild	Severe	Variable	NIL
Death of Dam	No	Yes(1)	No	No
Abortions	No	Yes(1)	Yes	No
Foetal resorption	Yes(1)	Yes(1)	No	No
Dystocia	No	No	No	No
Lambing	No	No	No	Yes
Parasitaemia Range	0-4	0-4	0-4	Nil
Mean±SD	2.1±1.7	2.8±1.1	2.3±1.9	Nil
Rectal Temperature Range:-0C	39.1-41.2	38.1-41.6	38.2-39.8	38.2-39.4
Mean±SD-0C	39.8±1.7	39.5±1.2	38.8±0.4	38.8±0.3
Highest Value-pi	41.2	41.6	39.8	-
%PCV Values. Range	14.0-29.0	10.0-35.0	15.0-29.9	26.0- 40.0
Mean±SD	21.7±4.3	22.4±6.3	20.5±5.1	30.9±3.5
Lowest Value pi-%	14.0	10.0	15.0	-
Plasma Proteins Values(g/dl.). Range	5.0-7.7	4.9-9.3	5.8-8.2	6.1-8.0
Mean±SD	6.3±0.8	6.7±0.9	6.5±0.5	6.9±0.1
Lowest Value pi	5.0	4.9	5.8	-
Highest % Change in body weight	123.3	-30.4	-15.2	+16.0

Key **(-) Loss in body weights of ewes.**
(+) Increase in body weights of ewes.

Parasitaemia:

Onset of parasitaemia in the infected Yankasa and WAD ewes in first trimester of pregnancy was within 3-4 days pi. High levels of parasitaemia were observed in the infected Yankasa and WAD ewes within the first two weeks pi(Fig.3.1). Thereafter fluctuations in parasitaemia were observed until death or treatment of the ewes. One out of the six infected-WAD ewes had self cure from the infection(Fig 3.1b) after loosing the pregnancy through embryonic death by 33 days pi. As determined by analysis of the ewe's sera samples using *radioimmunoassay of progesterone technique*(Fig 3.1c).

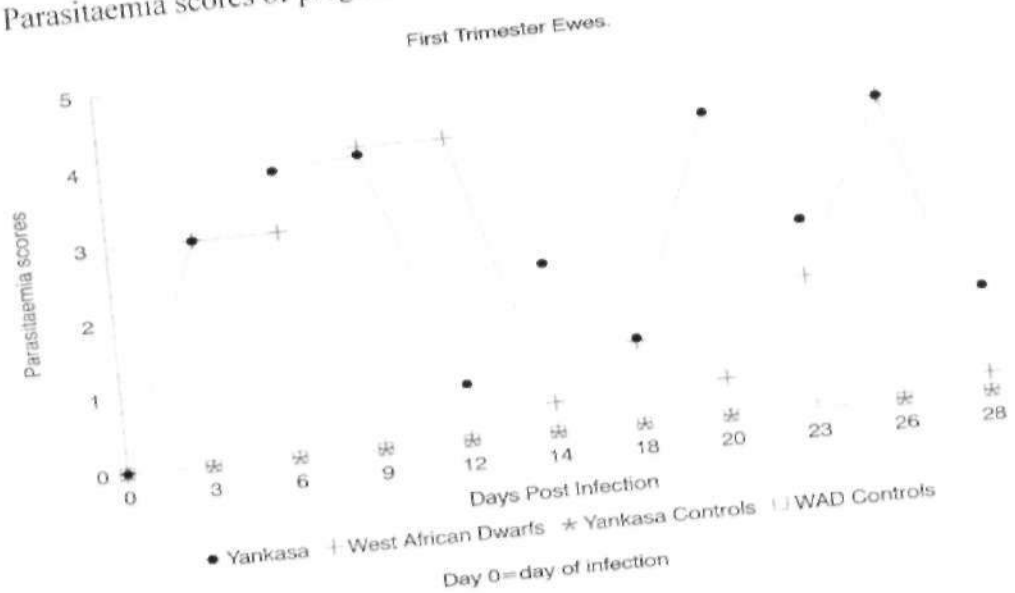
No significant ($P \geq 0.05$) differences were observed between the parasitemia levels of the infected Yankasa and WAD ewes(Appendix.1.1).

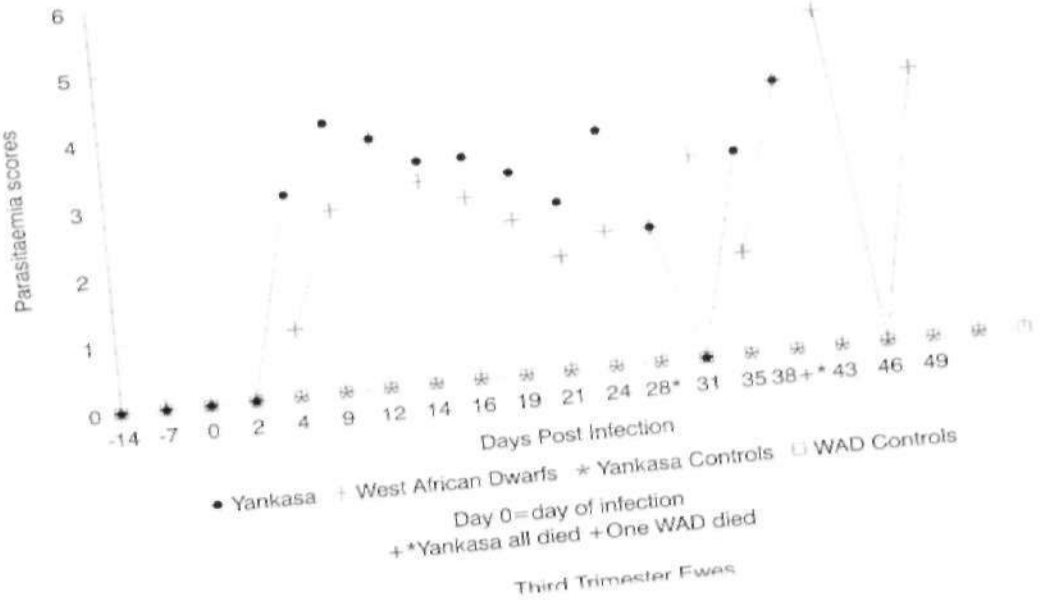
Rectal Temperatures:

Pyrexia was common in the infected ewes. It was high with the first wave of parasitaemia. Thereafter the ewes developed fluctuating pyrexia until death or treatment(Fig 3.2) The highest temperature recorded in the infected Yankasa ewes was 41.5°C with a mean of 39.6±1.7°C. The highest temperatures recorded in the infected WAD ewes was 41.2°C with a mean of 39.8±1.5°C.

Significant ($P \leq 0.05$) differences were observed between the rectal temperatures of the infected Yankasa and WAD ewes(Appendix.1.1).

Fig.3.1 Parasitaemia scores of pregnant Yankasa and WAD ewes infected with *T. vivax*





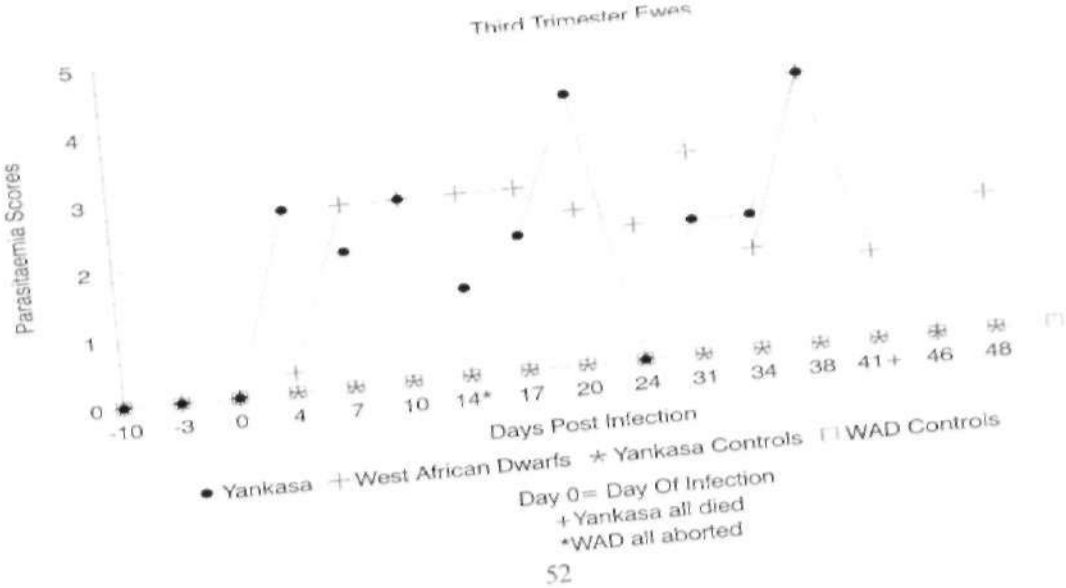
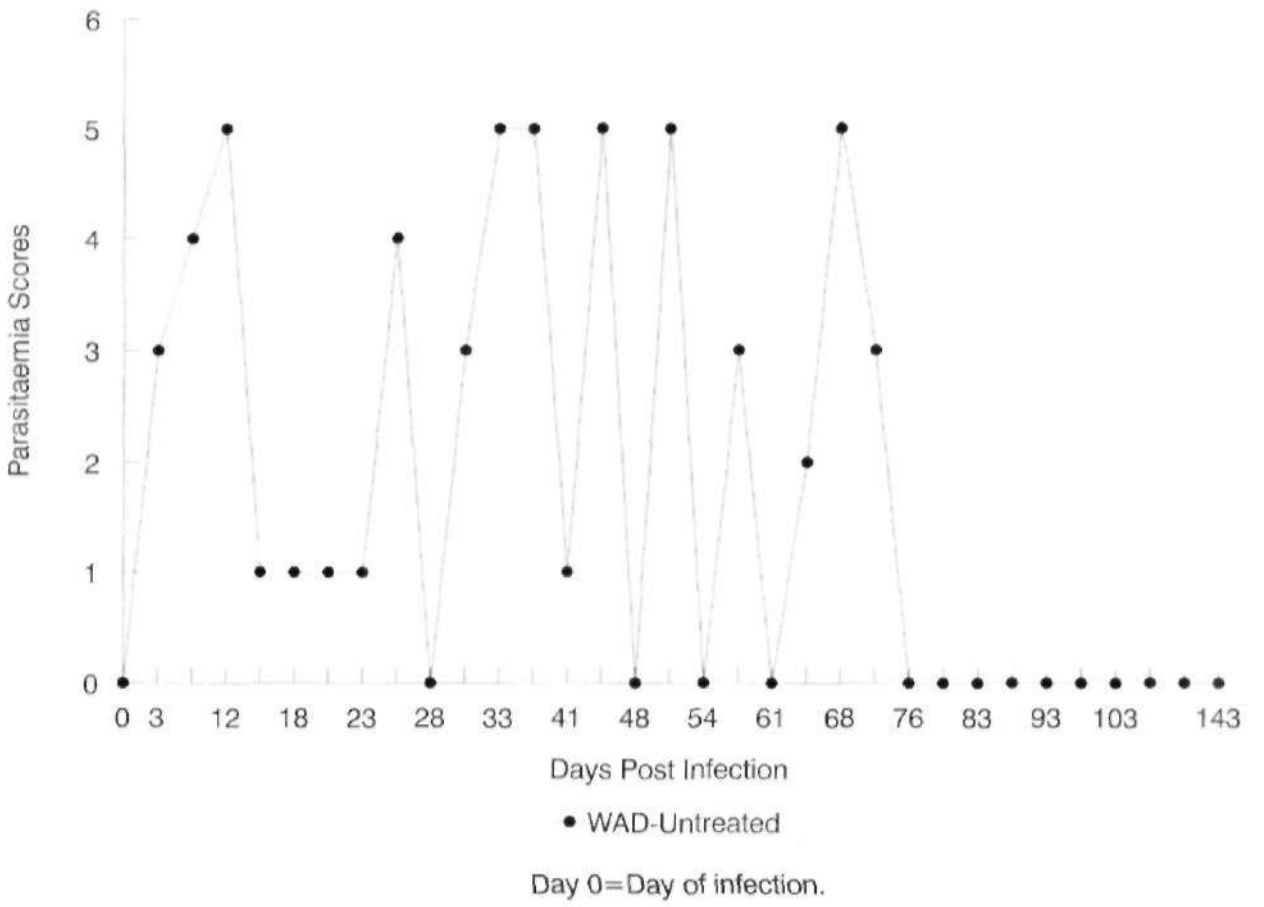
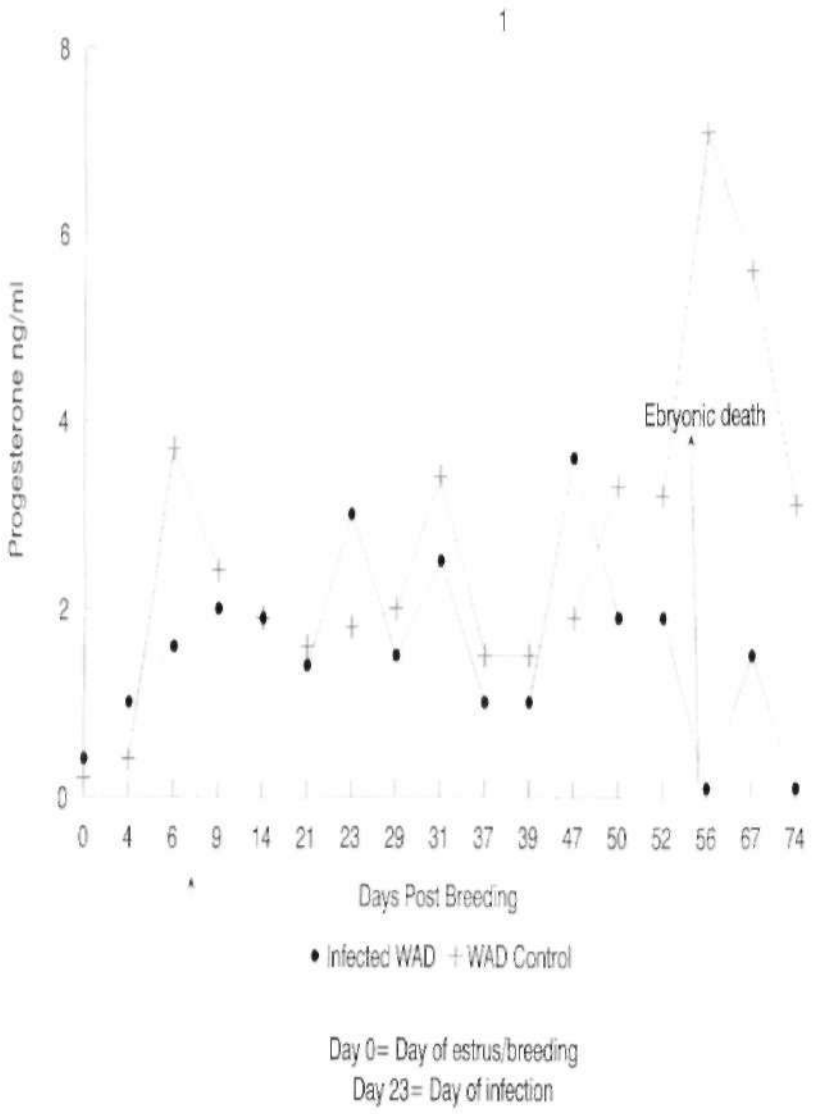


Fig 3.1b Parasitaemia scores of West African Dwarf ewe that had self cure from *T.vivax* infection.



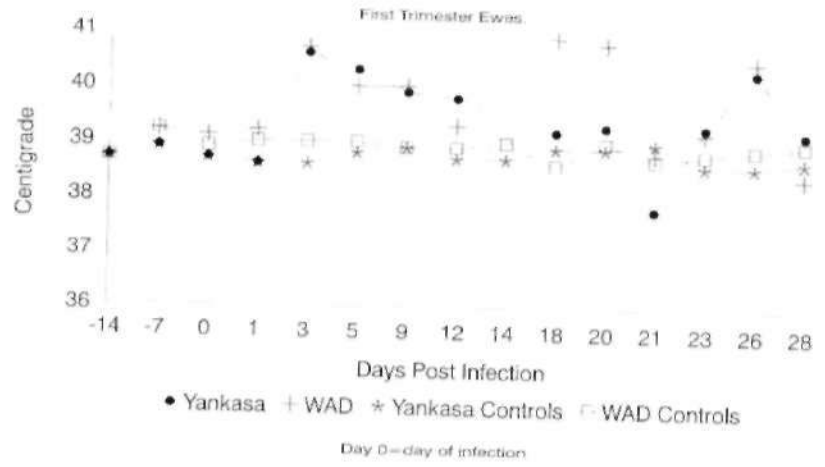
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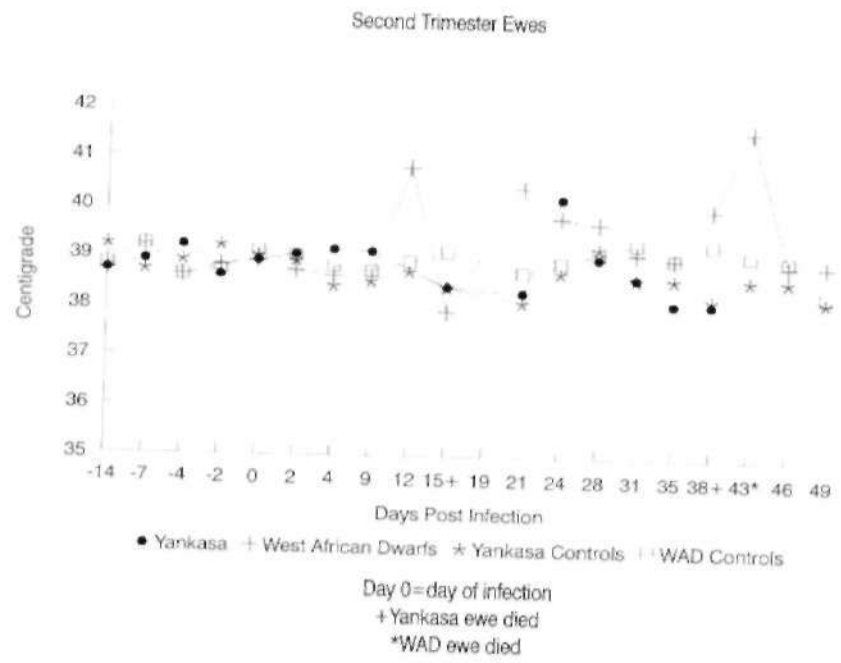
Fig 3.1c Progesterone profile of West African Dwarf ewe infected in the first trimester of pregnancy, that had embryonic death and self cure from the infection.

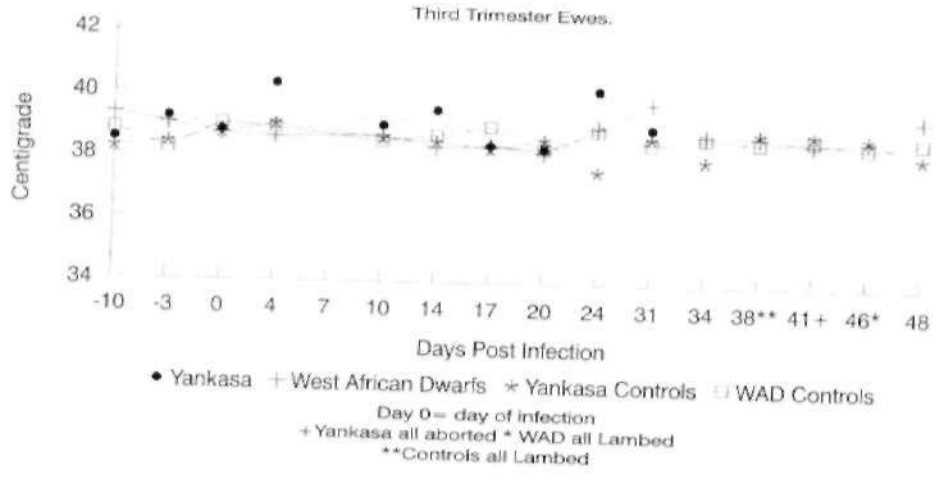


Day 0= Day of estrus/breeding
Day 23= Day of infection

Fig 3.2 Temperature scores of pregnant Yankasa and WAD ewes infected with *T. vivax*







Packed Cell Volume:

Packed cell volume (PCV) showed decline in the Yankasa and WAD ewes as from 5 days pi(Fig 3.3). The mean PCV value of the infected Yankasa ewes was 21.3±3.6%, range(15.0-29.0) (Table 3.1). The mean PCV value for the infected WAD ewes was 21.7±4.3%, range(14.0-29.0)(Table 3.2).

Significant ($P \leq 0.05$) differences were observed between the un-infected Yankasa and WAD control ewes and the infected Yankasa and WAD ewes. No significant ($P \geq 0.05$) differences were observed between the remaining treatment groups for PCV values(Appendix.1.1).

Changes in body weights(%):

The body weights of the infected Yankasa ewes, showed decline as from 6 days pi(Fig.3.4). The highest percentage decline in the body weights of the Yankasa ewes was -8.31%(Table 3.1), and was observed at 18 days pi. In the infected WAD ewes, the body weights increased rather than decline. The highest percentage increase in body weights of the infected WAD ewes was 23.3% and was observed at 28 days pi.

The percentage change in body weights of the un-infected Yankasa control ewes, was significantly ($P \leq 0.05$) different from that of the infected Yankasa ewes(Appendix.1.1). The un-infected WAD control ewes and the infected WAD ewes, were not significantly ($P \geq 0.05$)different, in body weights changes. 1).

Abortions:

One out of the six Yankasa ewes infected in the first trimester aborted 87 days pi, at 110 days of pregnancy. None of the WAD ewes infected in the first trimester aborted. Two out of the six infected WAD ewes had embryonic death by 13 and 33 days pi, respectively(Fig 3.1c). The foetuses were resorped.

Death from the infection:

All the Yankasa ewes infected in the first trimester died from the infection. None of the WAD ewes died from the infection.

SECOND TRIMESTER.

Clinical signs:

In the second trimester group, the infection was severe in the Yankasa than WAD ewes. The onset of the infection in the Yankasa ewes was early and characterized by massive parasitaemia, high pyrexia, lethargy, rough hair coats, enlarged prescapular lymph nodes, oral and nasal discharges, droopiness, anaemia and emaciation. Three out of the five severely affected Yankasa ewes developed severe diarrhea and signs of pneumonia. One of these three ewes, died from the infection at 11 days pi.

One of the six infected Yankasa ewes showed delayed onset of the severe clinical signs observed, until 28 days pi. This ewe died from the infection 10 days later, after developing severe clinical signs, similar to the other five infected Yankasa ewes. This ewe was the last of the Yankasa ewes infected in the second trimester to die.

In the WAD ewes, four out of the six ewes had delayed onset of clinical signs. Two out of the six infected WAD ewes, showed early and similar clinical signs as observed in the Yankasa, but with no diarrhea or signs of pneumomia. The other WAD ewes had delayed onset of clinical signs, until 38 days pi. All the WAD ewes eventually developed severe clinical trypanosomosis as the Yankasa ewes. Diarrhea or signs of pneumonia were however not observed. Also none of the WAD ewes died very early in the infection as observed in the Yankasa.

Parasitaemia:

Onset of parasitaemia in the infected Yankasa and WAD ewes was within 3-4 days pi. One WAD ewe had delayed onset until 9 days pi. High levels of parasitaemia were observed in the infected Yankasa and WAD ewes for the first three weeks of infection, thereafter fluctuations were observed(Fig.3.1).

Between the infected Yankasa and WAD ewes, no significant differences ($P \geq 0.05$) were observed in parasitaemic levels (Appendix 1.2).

Rectal Temperatures:

Pyrexia was common to all the infected Yankasa and WAD ewes. The pyrexia was high during the first wave of parasitaemia, thereafter the ewes developed fluctuating pyrexia until death or treatment(Fig 3.2). The onset of pyrexia in both the infected Yankasa and WAD ewes in the second trimester, coincided with the onset of parasitaemia and other clinical manifestations of the infection.

The highest temperatures recorded in the infected Yankasa and WAD ewes were 41.3°C(Table 3.1) and 41.6°C(Table 3.2) respectively. The rectal temperatures of the infected Yankasa and WAD ewes and the un-infected Yankasa and WAD ewes, were not significantly ($P \geq 0.05$) different(Appendix 1.2).

Packed Cell Volume:

Severe decline in PCV values were observed in the infected Yankasa and WAD ewes from 9-35 days pi. Thereafter the PCV values of the WAD ewes showed increase towards pre-infection levels(Fig. 3.3). The lowest PCV value observed in the infected Yankasa ewes was 11.0%(Table 3.1). It was observed in the last surviving infected Yankasa ewe on the the day it died at 38 days pi. The lowest PCV value observed in the infected WAD ewes, was

10.0%. It was observed 35 days pi, in the only WAD ewe that died from the infection 42 days pi.

The PCV values of the un-infected and infected ewes of both breeds, were significantly different($P \leq 0.05$) (Appendix 1.2). Significant ($P \leq 0.05$) differences were also observed between the infected Yankasa and WAD ewes (App. 1.2). The PCV values of both breeds were also significantly ($P \leq 0.05$) different, with Yankasa having PCV value of 17.26 $\pm$ 1.38 compared with WAD 23.52 $\pm$ 1.38(Appendix 1.2).

Changes in body weights(%):

The highest percentage decline in body weights in the Yankasa ewes was-23.0% and was observed by 28 days pi(Table 3.1). In the WAD ewes, it was 30.4% and was observed by 43 days pi(Table 3.2).

Between the Yankasa and WAD control ewes and the infected Yankasa and WAD ewes, significant ($P \leq 0.05$) differences were observed(Appendix1.2). However, no significant ($P \geq 0.05$) differences were observed between the infected Yankasa and WAD ewes(Appendix 1.2).

Abortions:

One infected Yankasa and one infected WAD ewe in the second trimester aborted. The abortions, coincided with periods of persistent high parasitemia and pyrexia.

Death from the infection:

Only one out of the six infected WAD ewes died from the infection at 42 days pi. In contrast all the infected Yankasa ewes died from the infection. The WAD ewe that died from the infection showed persistent high parasitaemia(3-4+) and pyrexia(39.5-40.1) from 35-42 days pi. The ewe died possibly from complications of dystocia. All the Yankasa ewes were dead from the infection by 38 days pi.

THIRD TRIMESTER.

Clinical signs:

The onset of the clinical signs in infected Yankasa ewes in the third trimester group, were very severe from onset in most of ewes. The signs observed were similar to those of the infected Yankasa ewes in the second trimester, except that there was no diarrhea or signs of pneumonia, as observed in some of the Yankasa ewes in the second trimester. Two out of the six Yankasa ewes aborted at 12 days pi and died few days later. One Yankasa ewe died without aborting at 10 days pi.

In the WAD ewes, the onset of clinical signs were severe in three out of the six infected WAD ewes. These ewes also aborted, one each at 12, 13 and 14 days pi, but none died after aborting. The remaining three infected WAD ewes, showed mild signs of the infection, characterized by fluctuating parasitaemia and pyrexia, lethargy, raised hair coats and enlarged prescapular lymphnodes.

Parasitaemia:

In the third trimester, the onset of parasitaemia was within 4 days pi, in the Yankasa and 7 days pi, in the WAD ewes. High levels of parasitaemia were observed in the infected Yankasa and WAD ewes, within the first three weeks of infection(Fig.3.1). Thereafter fluctuations in parasitaemia were observed in all the ewes. Between the infected Yankasa and WAD ewes, no significant ($P \geq 0.05$) differences were observed in parasitaemic levels *(Appendix.1.3;1.3.10)*.

Rectal Temperatures:

Pyrexia was common to all the infected ewes. The pyrexia was marked in the first wave of parasitaemia. Thereafter the ewes developed fluctuating pyrexia(Fig 3.2), until death or treatment. The highest temperatures recorded in the infected Yankasa ewes was

40.9°C(Table 3.1) and in the WAD ewes 39.8°C(Table 3.2).

The onset of pyrexia in both the Yankasa and WAD ewes coincided with the onset of parasitaemia and other clinical manifestations of the infection. The abortions observed in the infected Yankasa and WAD ewes, coincided with periods of persistently high parasitemia and pyrexia in the ewes. The rectal temperatures of the infected Yankasa and WAD ewes were not significantly($P \geq 0.05$) different(Appendix.1.3).

Packed Cell Volume:

Severe decline in PCV values were observed in the infected Yankasa ewes until death of the ewes. The WAD ewes controlled the decline in PCV values by 34 days pi.(Fig. 3.3). The lowest PCV value in the infected Yankasa ewes was 10%(Table 3.1) and was observed 31 days pi. In the infected WAD ewes, it was 15.0%(Table 3.2) and was observed 38 days pi.

The PCV values of the un-infected Yankasa and WAD control ewes, were significantly ($P \leq 0.05$) different from those of the infected Yankasa and WAD ewes(Appendix 1.3). The PCV values of the infected Yankasa and WAD ewes were not significantly ($P \geq 0.05$) different.

Changes in body weights(%):

The infected Yankasa ewes in third trimester of pregnancy showed rapid decline in body weights reflected by 35.5% drop 46 days pi, whereas gradual decline in body weights were observed in the WAD ewes, reflected by 15.2% drop 46 days pi.

Significant ($P \leq 0.05$) differences were observed between the infected Yankasa and WAD ewes(Appendix 1.3). Significant ($P \leq 0.05$) differences were also observed between the two breeds of ewes(Appendix 1.3.40).

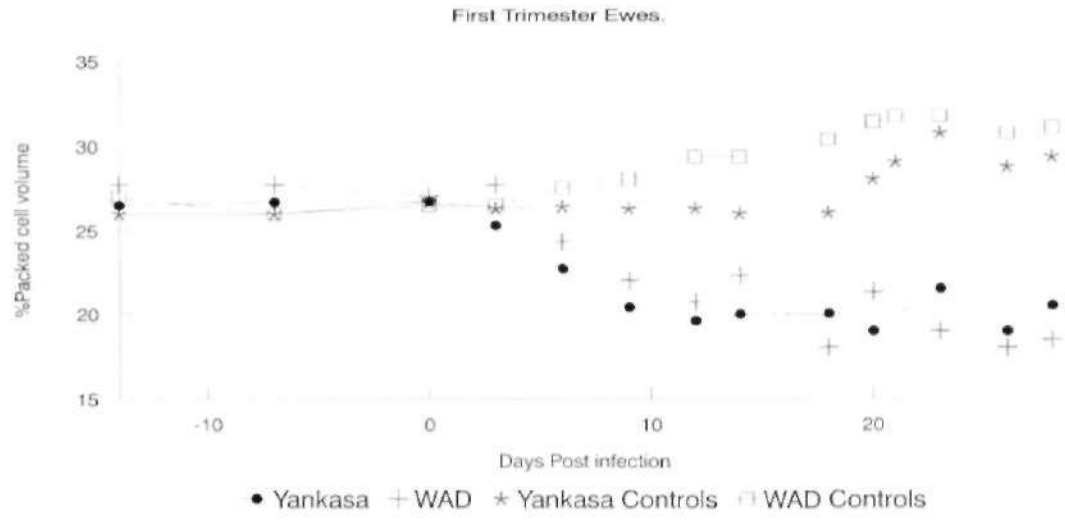
Abortions:

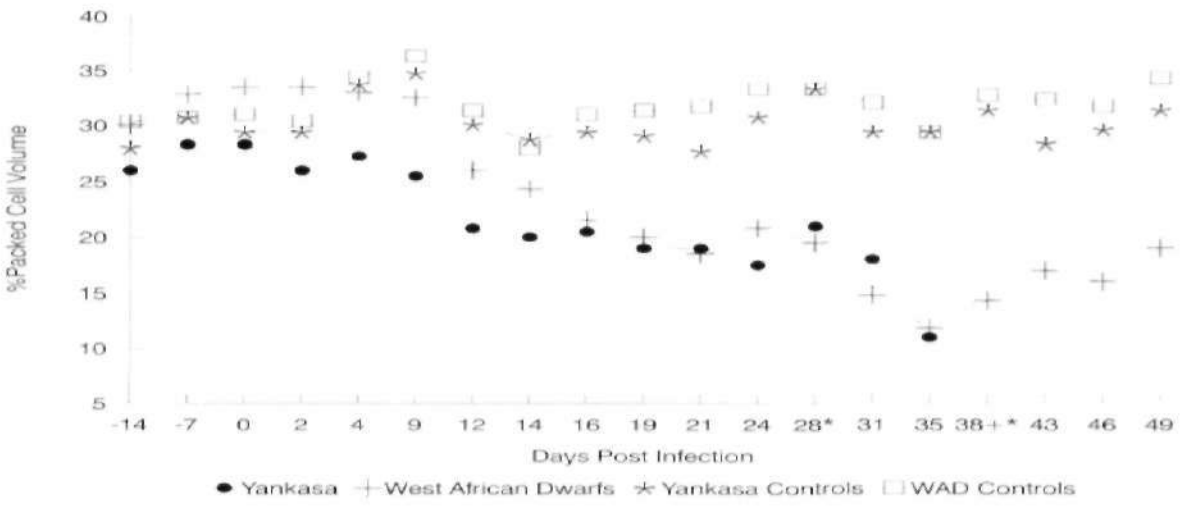
Four out of the six infected Yankasa ewes aborted and one had dystocia. In the WAD ewes three out of the six aborted.

Death due to the infection:

All the infected Yankasa ewes died from the infection. Four died after aborting, one died without aborting and one died from dystocia. None of the WAD ewes died from the infection.

Fig.3.3 Percent packed cell volume (PCV) scores of Pregnant Yankasa and WAD ewes infected with *T. vivax*





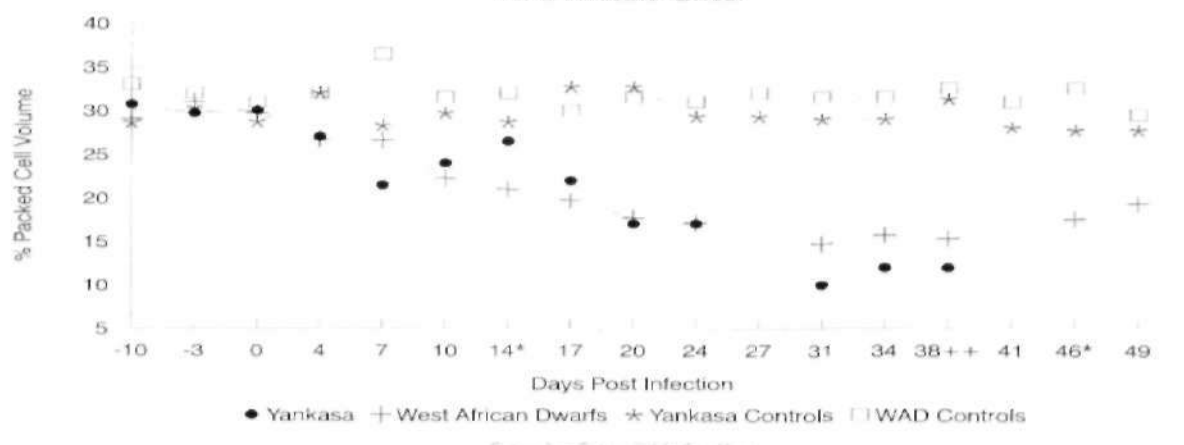
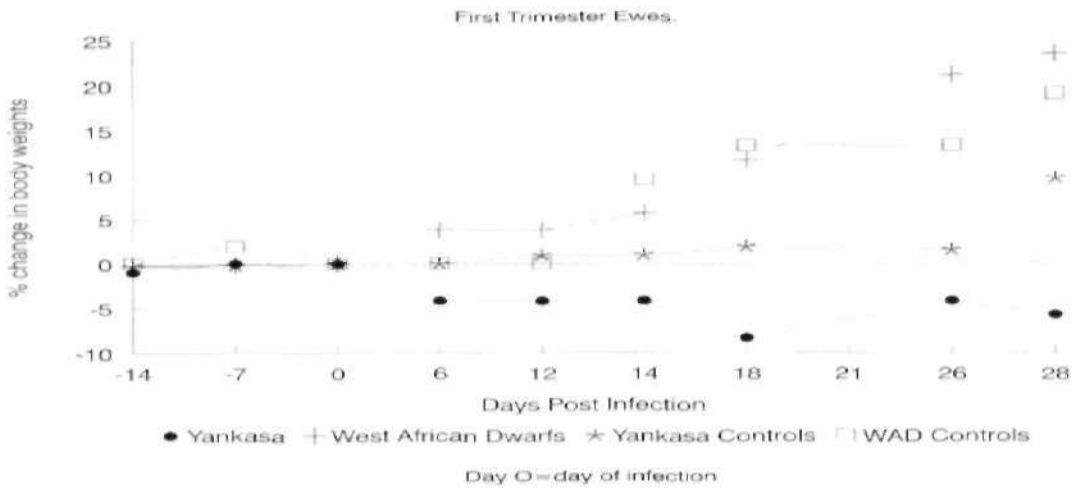
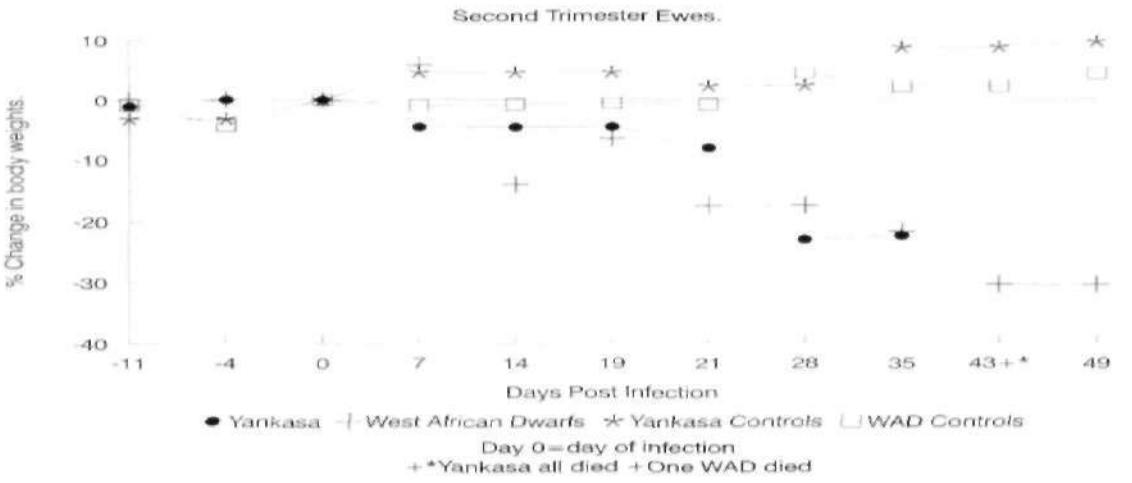
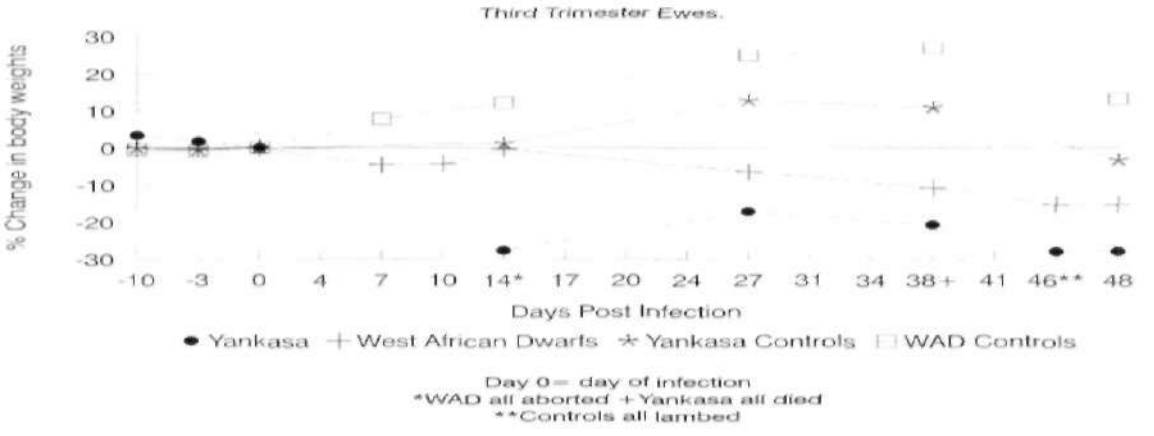


Fig.3.4 Percentage changes in body weight of pregnant Yankasa and WAD ewes infected with *T. vivax*







3.5 DISCUSSION

The results of the present study showed that both Yankasa and WAD ewes are susceptible to *T. vivax* infection. The study also showed that the severity and course of the infection was influenced by the stage of pregnancy and breed of ewe. In the Yankasa ewes, the severity of the infection increased as pregnancy advanced. This finding in Yankasa ewes agree with those of Ogwu (1983) in susceptible Zebu cattle.

In the WAD ewes a different picture was observed. The severity of the infection did not strictly increase as pregnancy advanced. WAD ewes infected in second trimester showed the most severe signs of the infection than those in the third trimester. Even though stormy abortions were observed in the WAD ewes in third trimester. The severe signs of anaemia and emaciation observed in the WAD ewes in the second trimester, were not observed in the third trimester and death did not occur in the third trimester following infection in this breed.

Individual variations in susceptibility similar to those reported in cattle (Desowitz, 1959; Margaret *et al*., 1988) were also observed in both the Yankasa and WAD ewes infected in second and third trimesters of pregnancy.

High peaks of parasitaemia early in the infection were observed in both the Yankasa and WAD ewes infected in all the stages of pregnancy and this agrees with previous observation in Zebu cattle (Ogwu *et al*., 1986). The WAD ewes however showed better ability in controlling the parasitaemia than the Yankasa. One WAD ewe infected in the first trimester also had self cure from the infection. The ability to control parasitaemia has been attributed to tolerance (Murray, 1987) and is also linked with the ability to mount effective and consistent immune response by the animal, which is antibody mediated (Luckins, 1976).

Consistently elevated IgM levels are reported in Trypanotolerant Ndama cattle, infected with trypanosomes (Desowitz, 1959; Luckins, 1976). IgM is reported more effective

than IgG at neutralizing, agglutinating and lysis of trypanosomes *in vitro* and providing protection *in vivo* (Seed 1972; 1977; Takayanagi and Enriquez,1973; Luckins, 1976; Musoke *et al.*,1981). Studies on homozygous athymic mice(nu/nu), which are devoid of mature T-cells and can only show IgM response. Confirmed the efficacy of IgM in controlling trypanosome infections(Campbell *et al.*,1978. Although various antibody levels were not determined in this study, the ability of the WAD ewes to limit anaemia and also control parasitaemia can be associated with the ability of the WAD ewes to mount effective antibodies mediated immune response than the Yankasa to control the infection.

Anaemia which is reported common in trypanosomosis of sheep(Anosa and Isoun,1974) was common to both the Yankasa and WAD ewes infected in second trimester of pregnancy. Even though anemia was common to both Yankasa and WAD ewes in the second trimester, significant($P \leq 0.05$)differences in PCV values were observed between the infected Yankasa and WAD ewes. With the latter having higher mean PCV value of 23.52±1.38), than the infected Yankasa (17.26±1.38). This showed that WAD ewes were able to tolerate the anemia better than Yankasa.

The behavior of the WAD ewes with regards to the anaemia by limiting the decline in PCV values in the second and third trimesters of pregnancy, better than the Yankasa and also showing recovery in PCV values towards pre-infection values, showed that the WAD ewes were tolerant to anaemia and likely have a tolerant trait that controls anaemia. This finding gives credence to reports by Murray (1987), who attributed the ability to resist anaemia as a tolerant trait to trypanosomosis inherent in Trypanotolerant livestock. Esievo *et al.*,(1986), reported that Trypanotolerant Ndama cattle have higher sialic acid concentration than Zebu cattle, suggesting that Ndama cattle require a much higher trypanosome parasitaemia than zebu cattle to achieve the same degree of anaemia. The

ability of the WAD ewes to control anaemia better than the Yankasa may be attributed to higher concentration of sialic acid on their erythrocytes.

The severity of the anemia in the infected Yankasa and WAD ewes at each stage of pregnancy, corresponded with the severity of the infection at that stage of pregnancy, as measured by levels of parasitaemia and pyrexia, decline in PCV values, clinical signs, loss in body weights and death of ewes. This finding gives credence to Anosa and Isoun (1974) report, that the severity of anaemia observed in *T. vivax* infected sheep and goats was related to the severity of the infection. Dargie *et al.*,(1979), also reported that the severity of anemia in cattle trypanosomosis is related to the intensity and duration of the parasitaemia.

Ruminants infected with *T. vivax* have been reported to have either failed to gain weight, lost weight or had reduced growth rate, compared with the un-infected animals (Edwards *et al.*, 1956; Ogwu, 1983; Elhassan, 1987 and Lawani, 1989). In this study, loss in body weights was common in the infected Yankasa ewes in all stages of pregnancy and in the infected WAD ewes in second and third trimesters of pregnancy. The WAD ewes infected in first trimester of pregnancy however gained weights instead ,as well as the un-infected control ewes.

The severity of the infection and breed of ewes influenced the changes in body weights, in both the Yankasa and WAD ewes. The significant ($P \leq 0.05$) differences observed in the percentage changes in body weights, between the Yankasa and WAD ewes, infected in their first and third trimesters of pregnancy, showed that the WAD ewes were more tolerant to the pathogenic effects of *T. vivax* infection on body weights than the Yankasa.

Deaths due to the infection were common in the Yankasa ewes, infected in the second and third trimesters of pregnancy. This may suggest that effective treatment against trypanosomosis during the first trimester of pregnancy, may be effective to carry the pregnant

Yankasa to term. Deaths due to the infection was only observed in one WAD ewe in second trimester of pregnancy that died at 42 days pi, after difficult abortion. This may suggest that the second trimester is the most critical period of pregnancy in the WAD ewes. The infected WAD ewes generally survived the infection after losing the pregnancy.

This study have shown that *T. vivax* infection in pregnant Yankasa ewes will most likely terminate in mortality, whereas mortality is rare in infected WAD ewes and WAD ewes will tolerate the infection once the stress of pregnancy is removed. This finding gives credence to earlier reports that pregnancy influences the susceptibility of animals to the pathogenic effects of trypanosomosis (Desowitz, 1959; Ogwu,1983; Margaret *et al.*,1988).

It is concluded from the present study that both pregnant Yankasa and WAD ewes are susceptible to *T. vivax* infection. Yankasa ewes in all trimesters of pregnancy were susceptible with those in the third trimester of pregnancy being most susceptible. WAD ewes in second and third trimesters of pregnancy were susceptible with those in the second trimester being most susceptible.

Yankasa and WAD ewes infected in first trimester of pregnancy were least susceptible to the infection and self cure from the infection was possible in infected WAD ewes during this stage of pregnancy. Survival and self-cure was possible in infected WAD ewes, after loosing their pregnancies which was not the case with the Yankasa. The study showed that pregnancy was a stress factor that increases the susceptibility of both Yankasa and WAD ewes to the pathogenic effects of *T. vivax* infection.

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4.0 CHAPTER FOUR

THE EFFECTS OF *Trypanosoma vivax* INFECTION AND NOVIDIUM[R] [HOMIDIUM CHLORIDE] CHEMOTHERAPY IN PREGNANT YANKASA AND WEST AFRICAN DWARF[WAD] EWES IN THEIR FIRST, SECOND AND THIRD TRIMESTERS OF PREGNANCY.

4.1 SUMMARY

Three groups of six pregnant Yankasa and six pregnant WAD ewes in each group, were assigned at random to first, second and third trimesters of pregnancy, to study the effects of *T. vivax* infection and Novidium(R)(homidium chloride) chemotherapy in pregnant Yankasa and WAD ewes in their first second and third trimesters of pregnancy. Three pregnant Yankasa and 3 WAD pregnant ewes uninfected, formed the controls for the study.

One case of partial resorption of foetus and one case of almost complete resorption of foetus were observed in the infected-untreated Yankasa ewes in the first and second trimesters of pregnancy respectively. Foetuses from infected-untreated ewes were lower in body weights than foetuses from infected-treated ewes. This was often observed in the infected-untreated Yankasa ewes foetuses than in the infected-untreated WAD ewes foetuses.

Abortions were observed in the infected-untreated Yankasa ewes in the second and third trimester. Foetal death in-utero and expulsion of dead autolysed foetuses were observed in the infected-treated Yankasa in the first and second trimester, while abortions and dystocia were observed in the third trimester.

Embryonic death and resorption of foetuses were observed in the infected-untreated WAD ewes in the first and second trimester. Abortions were observed in the infected-untreated WAD ewes in the second and third trimester. Delivery of healthy lambs were observed in the infected-treated WAD ewes in the second and third trimester.

It is concluded from the study that the pathogenic effects of *T.* vivax infection on pregnancy may not be completely ameliorated by Novidium(R) chemotherapy of pregnant Yankasa ewes, but are completely ameliorated in the WAD ewes, leading to normal

deliveries of lambs at term. Clinical *T. vivax* infection of a short duration of 14 days, was enough to cause irreversible pathology in pregnant Yankasa ewes, leading to foetal resorption, abortions and dystocia which may not be ameliorted by Novidiun chemotherapy.

It was deduced from this study, that the tolerance of WAD ewes to trypanosomosis can be augmented by Novidium$^{(R)}$ chemotherapy to eliminate the pathogenic effects of trypanosomosis on pregnancy and may enhanced their productivity in areas endemic for trypanosomosis.

4.2 INTRODUCTION

The effects of both haematic and tissue trypanosomes on female reproduction have been reported by several investigators. Abortions during various stages of pregnancy and neonatal mortalities have been described in cattle(Boyt, 1971; Fio-Ngaindiro, 1987; Ogwu *et al*., 1986; Ogwu and Njoku, 1987; Sekoni, 1994) and in sheep infected with *T. vivax* (Elhassan, 1987; Bawa *et al*., 1990. Akinbamijo *et al*., 1994).

Pyrexia has been described to have detrimental effects on ovarian and tubal function (Ogwu *et al*., 1984), and to cause abortions in pregnant WAD ewes infected with *T. vivax,* in the first and third trimesters of pregnancy (Elhassan, 1987). Stress induced by pyrexia has been shown to activate foetal hypothalamo-pituitary-adrenal axis, to produce corticosteroids from the adrenal gland (Tilton *et al*, 1972). These corticosteroids are said to stimulate the production of prostaglandin F2 alpha and oestrogen from the placenta. The prostaglandin F2 alpha initiates abortion by reducing myometrial activity threshold, and concentration of progesterone through corpus luteolysis, while oestrogen causes uterine contraction and foetal expulsion(Liggins *et al*., 1972).

Genital lesions have been described in trypanosoma infections in cattle(Moulton and Sollod, 1976; Ogwu *et al*., 1984; Ogwu and Njoku, 1991). These lesions have been reported to make conception impossible, through the occlusion of the tiny lumen of the uterus, through acute and proliferative swellings (Jones and Hunt, 1983).

Trypanosomosis is one of the most important livestock diseases in Sub-Saharan Africa and chemotherapy has been employed for decades, as one of the measures for the control of the infection. Hence the heavy dependence of the livestock industry in Nigeria and Africa in general on drugs for both chemotherapy and chemoprophylaxis of the infection[ILRAD,1990]. Despite these measures, little has been achieved in the control of

trypanosomiasis and its effects on animal productivity in Africa. Consequently, the objective of this study was to determine the effects of Novidium$^{(R)}$ [Homidium Chloride] chemotherapy on *T. vivax* infection in pregnant Yankasa and WAD ewes in their first second and third trimesters of pregnancy.

4.3 MATERIALS AND METHODS

The selection of animals, experimental design and infection of the ewes, are as described in chapter three.

TREATMENT:-

Fourteen days pi, the infected Yankasa and WAD ewes in each of the trimester groups, were divided into two groups made up of 3 pregnant Yankasa and 3 pregnant WAD ewes in each group. One group was treated with Novidium$^{(R)}$ at 1.0 mg/kg body weight, while the other group remained untreated. The degree of anaemia as determined by PCV values and/or the severity of clinical signs were used in determining the ewes for treatment. Ewes with low PCV values in the group and/or with most severe clinical signs were selected for treatment. Relapsed infections were treated again.

Following treatment at 14 days pi, closely identical pairs(by weight) of infected-treated and infected-untreated Yankasa and WAD ewes in each of the trimester groups, were sacrificed at 21 days pi and at the end of each trimester of pregnancy, for comparative studies of the effects of treatment on foetal weights. The remaining pair of untreated and treated Yankasa and WAD ewes, in the three trimester groups were allowed to carry their pregnancies to term if possible. Ewes that died from the infection before the scheduled days for treatment or sacrifice were thoroughly examined at post-mortem.

The ewes were monitored daily post infection, for signs of anaemia. While PCV, rectal temperatures and parasitaemia were determined twice weekly and body weights taken weekly. Sera samples were collected from the ewes twice weekly for progesterone determination. The weights of the gravid uteri and foetus(es) were determined. The weights of the foetuses were also expressed as percentage of foetal weights [percentage foetal weight, is weight of the foetus expressed as percentage of dam's weight].

4.4 RESULTS

FIRST TRIMESTER

The clinical manifestation of the infection in the ewes, infected in the first trimester have been described in the previous chapter.

Foetuses:

The severity of the infection and breed of ewes, influenced the effects of treatment on foetuses body weights. In the first trimester when the infection was mild, low foetal body weight was only observed in one foetus from the infected-untreated Yankasa ewe sacrificed at 21 days pi. The foetus from the infected-treated ewe was higher in body weight and percentage foetal weight than the infected-untreated foetus. The foetuses from the infected-untreated and the infected-treated Yankasa ewes sacrificed at the end of the first trimester(28 days pi), were similar in body weights and percentage foetal weights(Appendix 2.1). Low foetuses body weights were not observed in the infected-untreated WAD ewes.

Embryonic death and resorption:

This was not observed in the infected-untreated and infected-treated Yankasa ewes in the first trimester but observed in one infected-untreated and one infected-treated WAD

ewe. The infected-treated WAD ewe had the embryonic death before it was treated at 14 day pi(Fig. 4.2). The infected-untreated WAD ewe also had self-cure from the infection(Fig 3.1b), after loosing the pregnancy. Both the infected-untreated and infected-treated WAD ewes resumed normal oestrous cycles, after loosing their pregnancies(Fig.4.1; Fig.4.2).

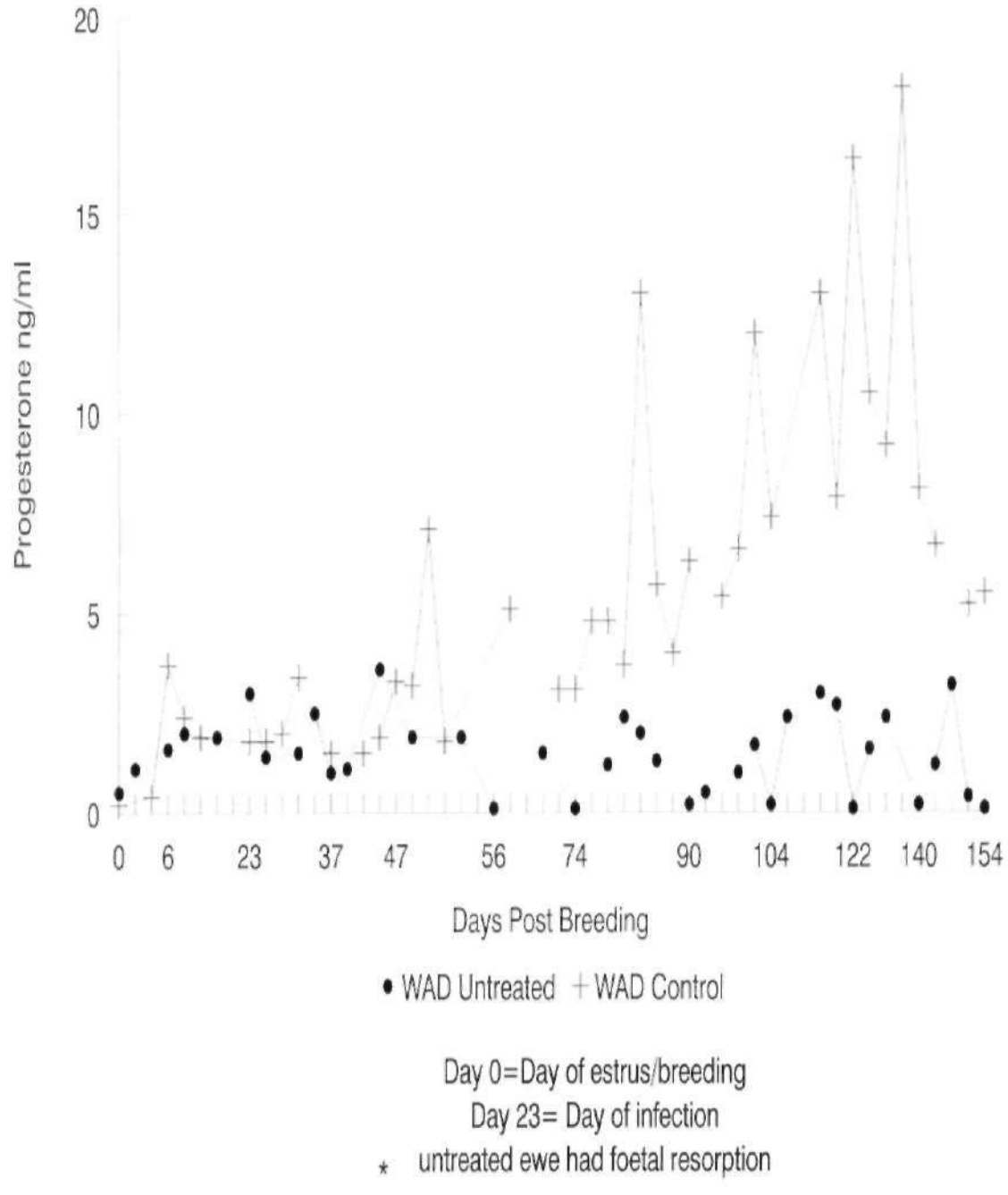
Pregnancy and delivery:

None of the infected-untreated and infected-treated Yankasa and WAD ewes in the first trimester, allowed to carry the pregnancy to term lambed. The infected-untreated Yankasa ewe died 41 days pi, at 64 days of pregnancy(Fig. 4.3). The foetus recovered from the ewe weighed 3.344gm (0.017%), and was already undergoing resorption from the limbs(Plate 4.2).

The infected-treated Yankasa ewe had four relapsed infections, between 14-25 days post treatment. Even though the relapsed infections were treated, the ewe aborted 87 days pi,at 110 days of pregnancy(Fig.4.4. The foetus died in-utero and was expelled autolyzed.

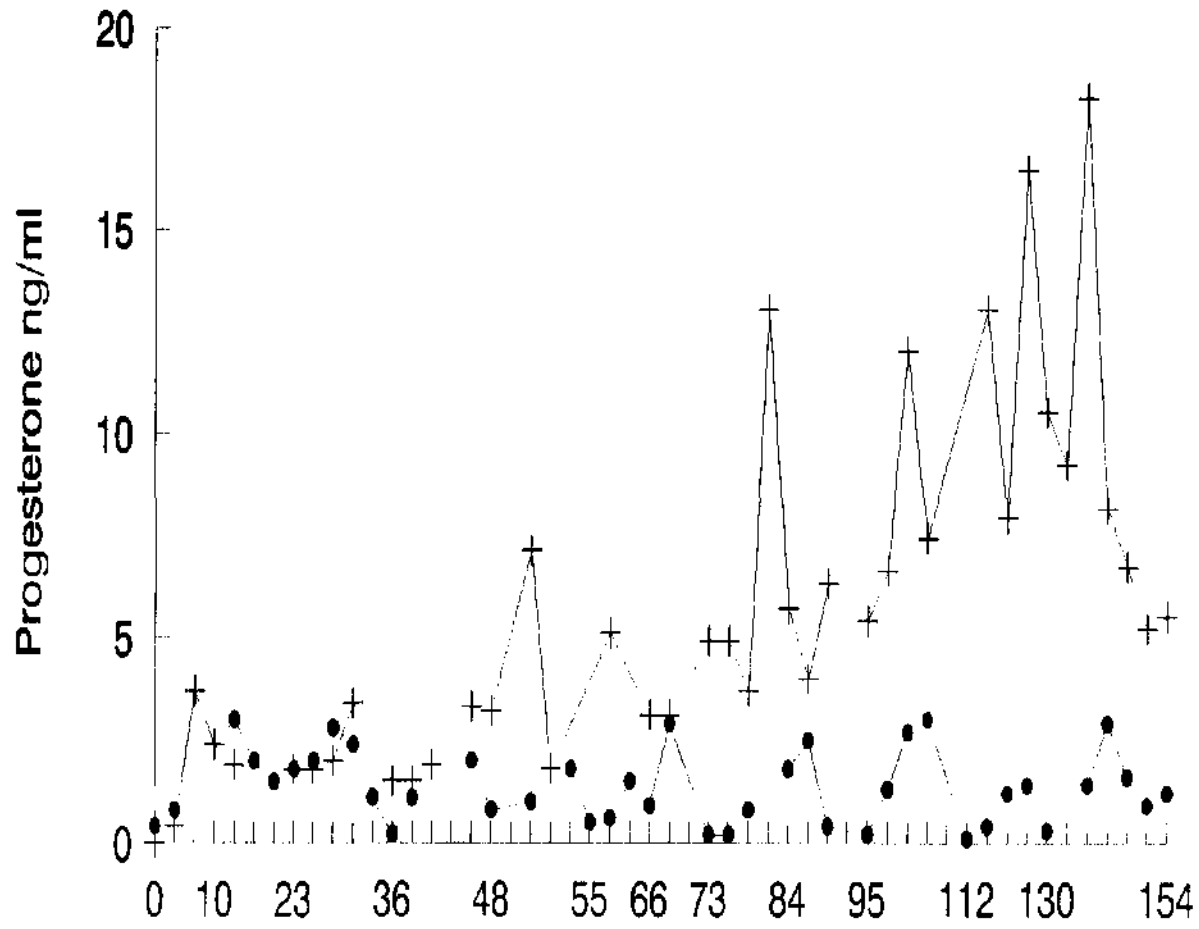
The infected-untreated WAD ewe, in the first trimester left to carry the pregnancy to term, had early embryonic death and resorption. The ewe also recovered form the infection(seif cure) and resumed normal estrous cycles(Fig 4.1). The infected-treated WAD ewe, left to carry the pregnancy to term, also had early embryonic death and resorption, before the ewe was treated at 14 days pi. The ewe resumed normal estrous cycle(Fig 4.2).

Fig 4.1 Progesterone profile of infected-untreated West African Dwarf ewe, infected in the first trimester pregnancy that had embryonic death, self cure from the infection and resumption of normal estrous cycles.



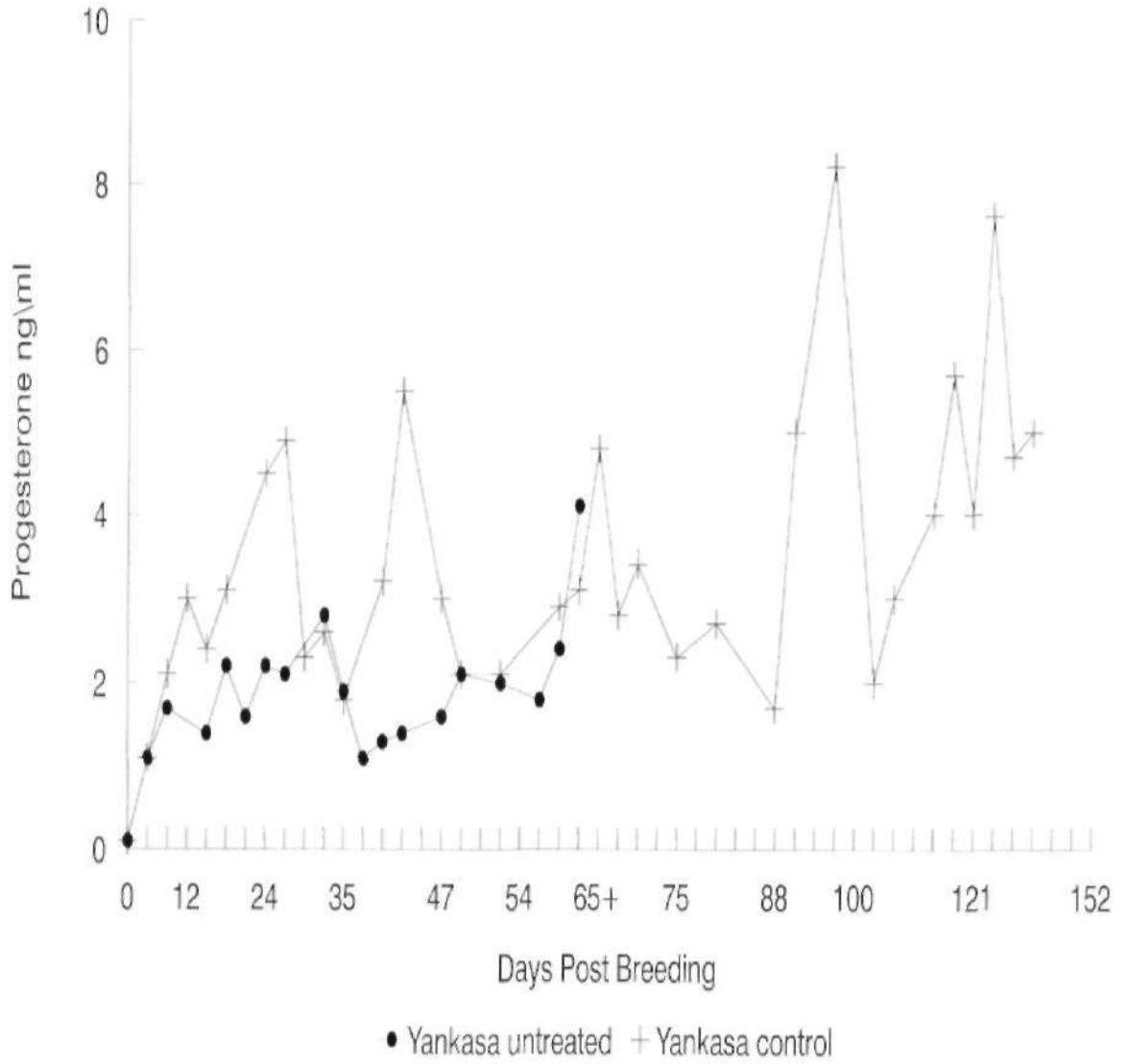
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Fig 4.2 Progesterone profile of infected –treated West-African Dwarf ewe, infected in the first trimester of pregnancy, that had embryonic death (before treatment) and also resumed normal estrous cycles.



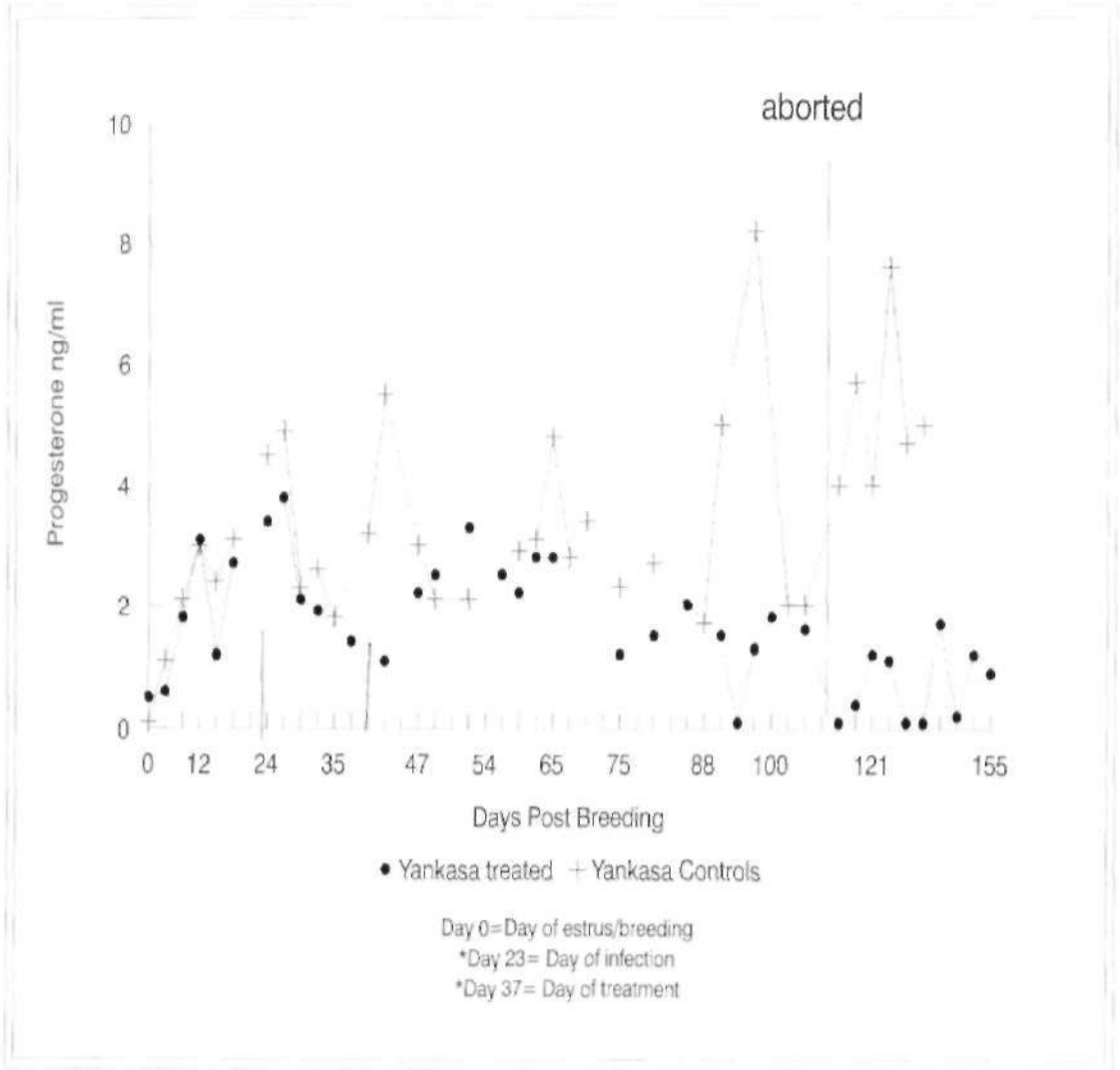
Day 0= Day of estrus/breeding
Day 23 = Day of infection
Day 37 = Day of treatment

Fig 4.3 Progesterone profile of infected-untreated Yankasa ewe, infected in the first trimester that died at 41 days pi, 64 days of pregnancy. The foetus recovered from the ewe was being resorbed from the limbs.



Day 0=day of estrus\breeding
Day 23- day of infetion
+Infected ewe died

Fig 4.4 Progesterone profile of infected-treated Yankasa ewe, infected in the first trimester of pregnancy that abortd a dead autolysed foetus at 87 days pi, 110 days of pregnancy.



SECOND TRIMESTER

The clinical manifestation of the infection in the ewes infected in the second trimester have been described in the previous chapter.

Foetuses:

The severe nature of the infection in both the Yankasa and WAD ewes, influenced the effects of treatment on the weights of the foetuses. Low foetal weights were in all the infected-untreated Yankasa ewes foetuses and in one infected-untreated WAD ewe foetus. The foetuses from the infected-untreated ewes, were lower in body weights and percentage foetal body weights, than the foetuses from the infected-treated ewes(Appendix 2.1; 2.2).

Pregnancy and delivery:

The severity of the infection and breed of ewe influenced the effects of treatment on pregnancy and delivery. The infected-untreated Yankasa ewe in the second trimester that was to carry the pregnancy to term, died during the acute phase of the infection 11 days pi, at 63 days of pregnancy. The foetus recovered from the ewe at post-mortem weighed 0.531mg and was almost completely resorbed(Plate 4.1), only the skull was clearly identifiable. The infected-treated Yankasa ewe left to carry the pregnancy to term, had three relapse infections between 21-43 days post treatment. The relapsed infections were treated. Despite the repeated treatments, the ewe aborted 54 days pi, at 106 days of pregnancy(Fig 4.5). The foetus died in-utero and was expelled autolyzed.

The infected-untreated WAD ewe in the second trimester died from the infection 41 days pi, possibly due to dystocia related complications. Two autolyzed foetuses were recovered from vaginal area of the ewe at post mortem.The infected-treated WAD ewe in the second trimester group, left to carry the pregnancy to term had normal delivery(Fig.4.6)

THIRD TRIMESTER.

In the third trimester group, the infection was very severe in the Yankasa. In the WAD ewes, it was severe in some and mild in others. The clinical manifestation of the infection in the Yankasa and WAD ewes, infected in the third trimester have been described in the previous chapter.

Foetuses, Pregnancy and delivery:

One infected-untreated Yankasa ewe died without aborting, while two aborted before dying between 9-12 days pi. Three infected-untreated WAD ewes aborted between 12-14 days pi. The aborted Yankasa ewes foetuses were similar in body weights and percentage foetal body weights(Appendix 2.1). The aborted WAD ewes foetuses were higher in percentage foetal body weights than the aborted Yankasa ewes foetuses(Appendix 2.1 and 2.2).

One of the infected-untreated Yankasa ewes that survived beyond 14 days pi, aborted 32 days pi, 138 days of pregnancy. The foetus recovered from the ewe weighed 910 gm (4.80%)(Appendix.2.1). One infected-treated Yankasa ewe aborted 23 days pi, 129 days of pregnancy. The foetus recovered from the ewe weighed 930gm(4.2%). Another infected-treated Yankasa ewe had dystocia 40 days pi, that was at 146 days of gestation, the foetus weighed 1.140kg (5.80%) (Appendix 2.1).

Three infected-treated WAD ewes successfully carried the pregnancies and lambed between 52-54 days of gestation. It was observed from the study that following treatment, the infected-treated WAD ewes in the third trimester of pregnancy stopped aborting and carried their pregnancies to term, without treatment being repeated in the ewes. In contrast, the infected-treated Yankasa ewes either aborted or had dystocia despite repeated treatment.

The Yankasa and WAD control ewes, carried their pregnancies to term and had normal deliveries. The WAD control ewes lambed earlier than the infected-treated WAD ewes. This was most apparent in the third trimester of pregnancy. The infected-treated WAD ewe in the third trimester that lambed last, also had the lamb with the lowest body weight (1.10kg)(Appendix 2.2).



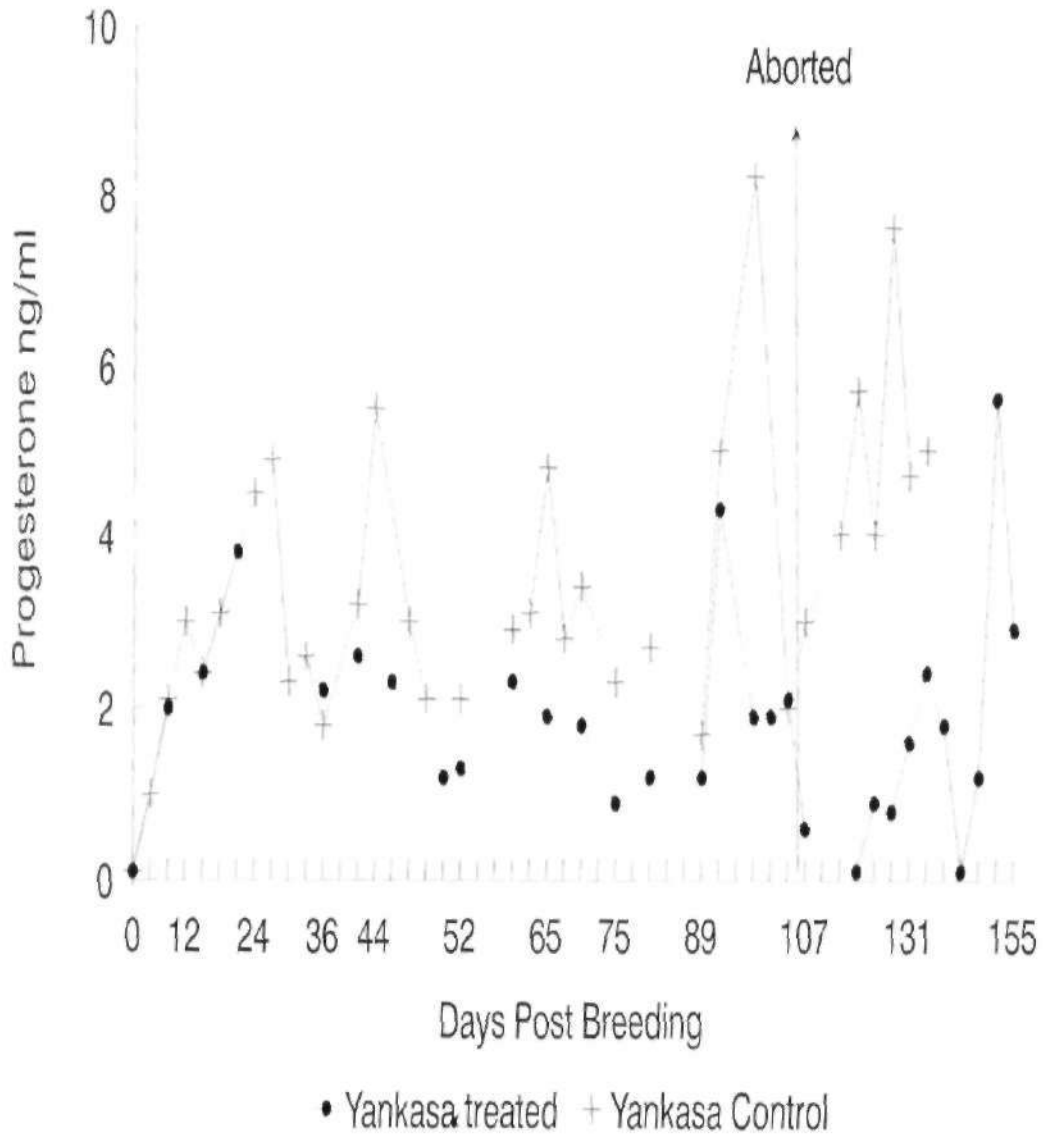
Plate 4.1 An almost completely resorbed foetus from a 63 days old pregnant Yankasa ewe, in second trimester of pregnancy that died acutely from *T. vivax* infection.



Plate 4.2. A Partially resorbed foetus[limbs] from a 64 days old pregnant Yankasa ewe in first trimester of pregnancy that died at 41 days post infection from *T. vivax* infection.

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Fig 4.5 Progesterone profile of infected-treated Yankasa ewe infected in the second trimester of pregnancy, that aborted a dead autolysed foetus at 54 days pi, 106 days of pregnancy.



Day 0= Day of estrus/breeding
Day 52= Day of infection
Day 66= Day of treatment

Fig 4.6 Progesterone profile of infected-treated West African Dwarf ewe, infected in the second trimester of pregnancy, that had normal delivery.

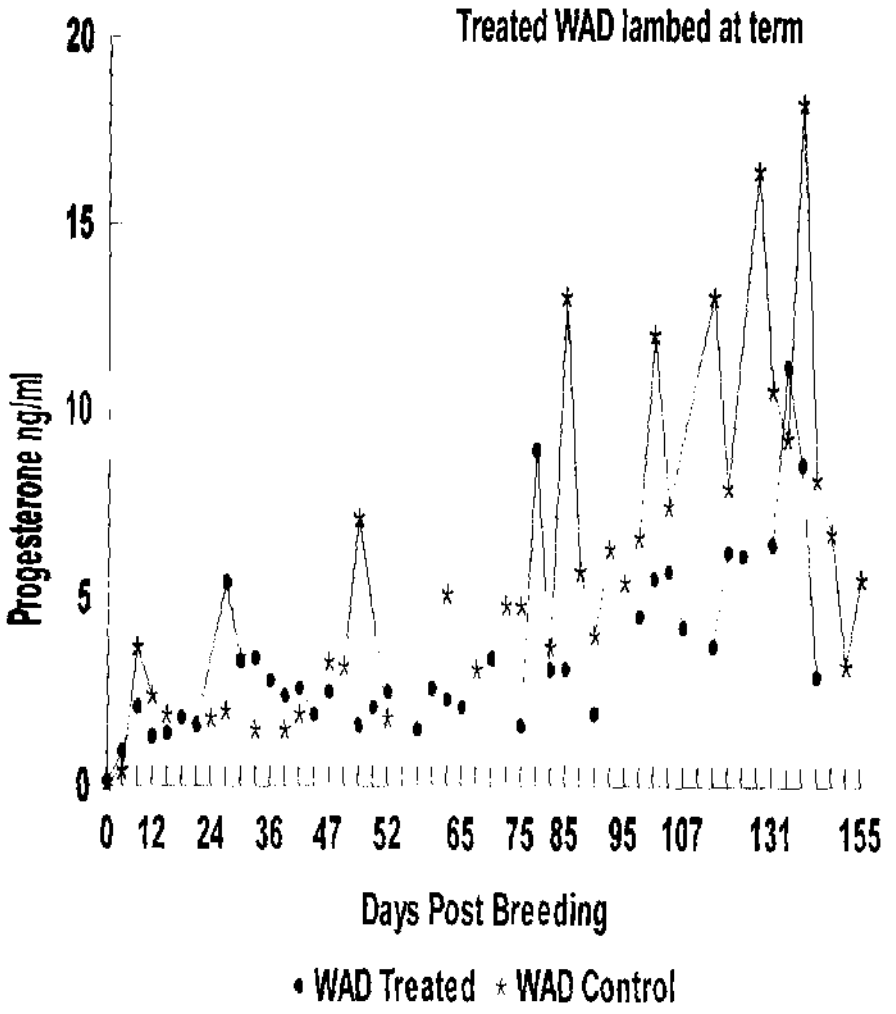


Fig 4.7 Progesterone profile of infected –treated Yankasa ewe infected in the third trimester of pregnancy, that aborted at 23 days pi, 129 days of pregnancy.

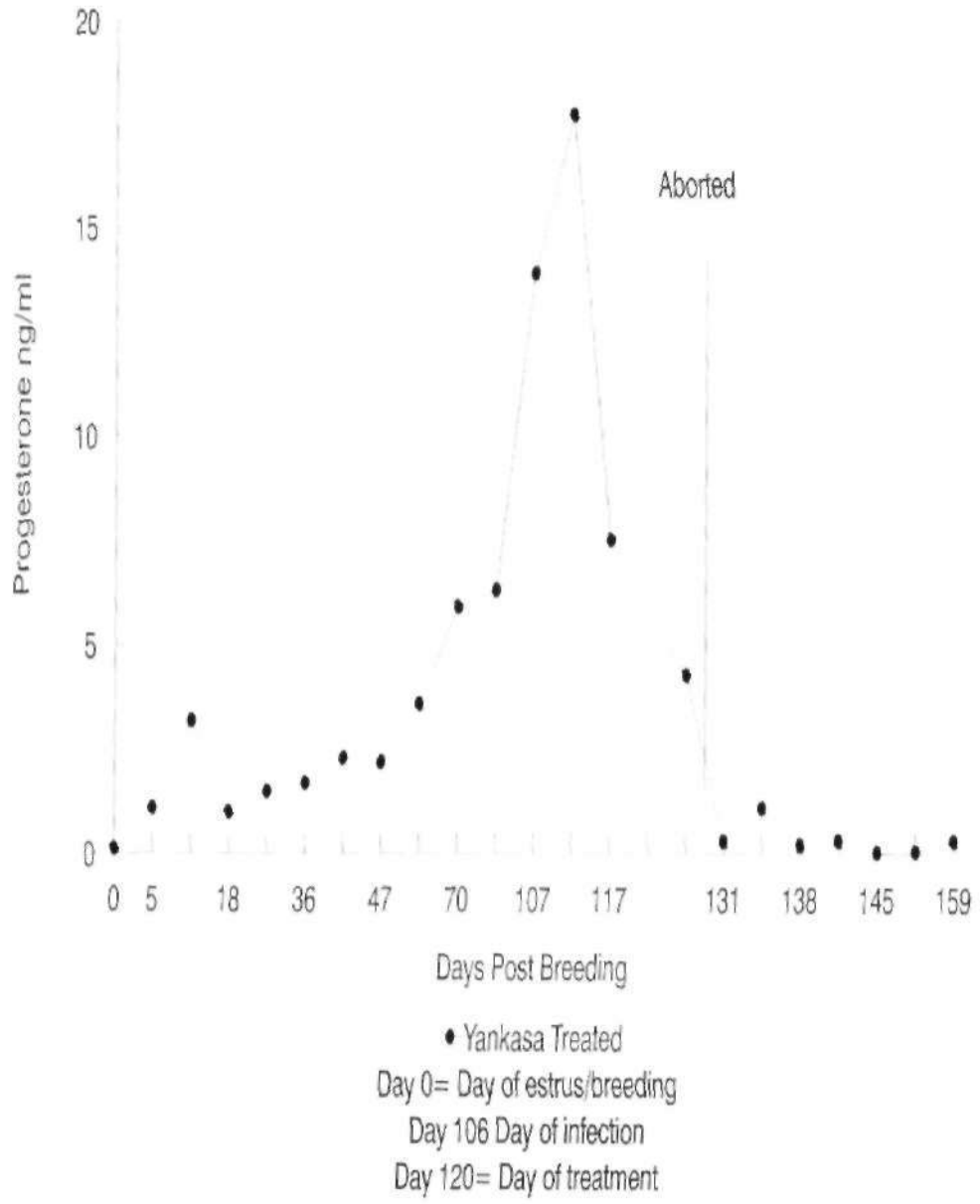
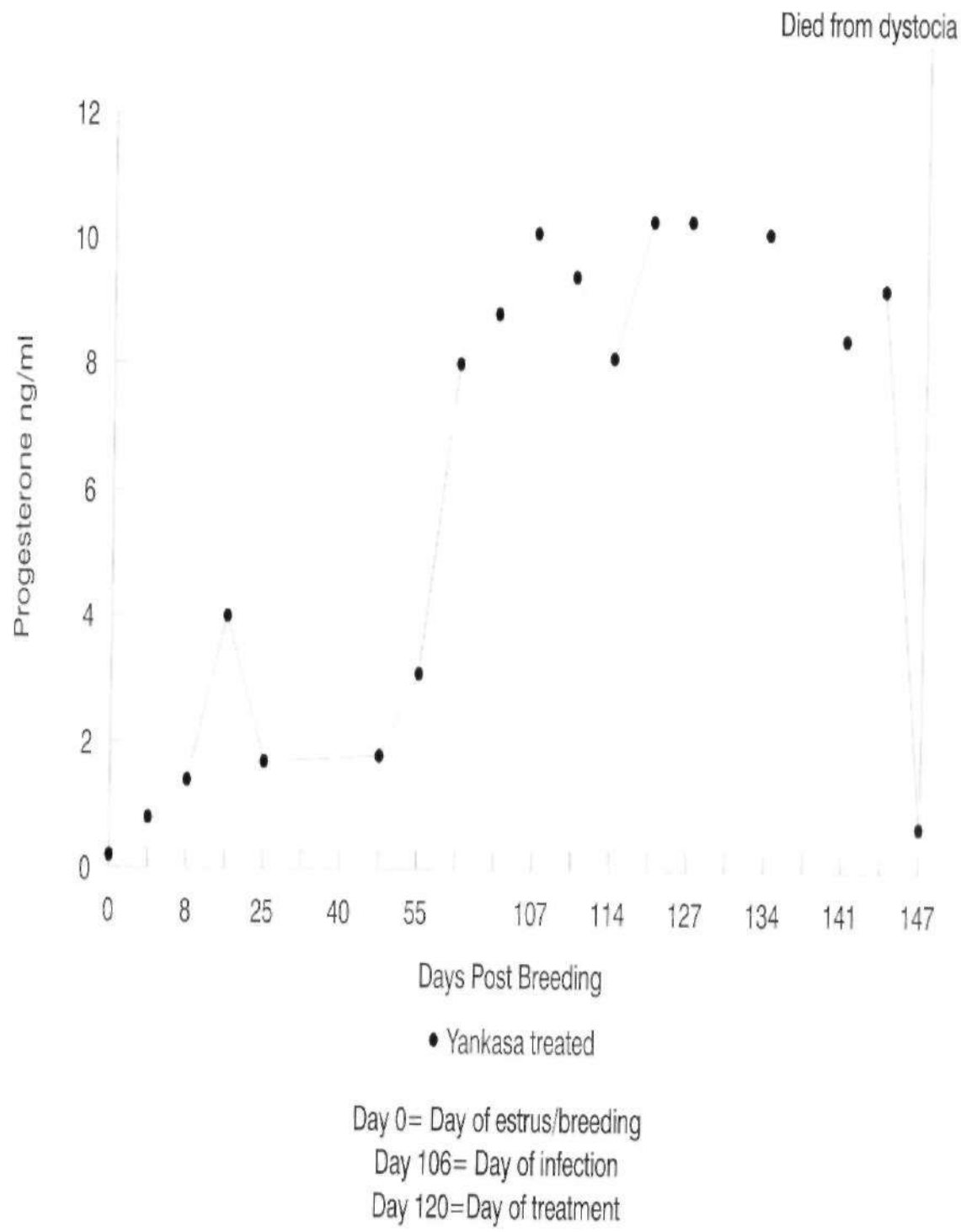


Fig 4.8 Progesterone profile of infected-treated Yankasa ewe, infected in the third trimester of pregnancy, that had dystocia at 40 days pi, 146 days of pregnancy.



4.5 DISCUSSION

All the infected Yankasa and WAD ewes in the three trimester groups developed clinical trypanosomosis. The severity and course of the infection in both breeds was influenced by the stage of pregnancy. Ewes in advanced pregnancies were most susceptible. Similar observations have been reported in cattle (Ogwu and Njoku, 1987). The breed of ewe influenced the outcome of the infection in the ewes.

The severity of the infection at each stage of pregnancy influenced the effects of the infection on body weights of the dams and the foetuses. In the first trimester group in which the infection was mild in both breeds, minimal decline in body weights were observed in the Yankasa ewes(8.31%), consequently, low foetal body weight was only observed in the Yankasa ewes in one foetus from the untreated Yankasa ewe sacrificed at 21 days pi. The infected-untreated WAD ewes showed increase in body weights(23.3%). Similarly low foetal body weights were not observed in the infected-untreated WAD ewe's foetuses.

In the second trimester group, in which the infection was both severe in the Yankasa and WAD ewes, severe decline in body weights were observed in both the Yankasa(23.0%) and WAD ewes(30.4%). Consequently low foetal body weights were observed in both the infected-untreated Yankasa and WAD ewe's foetuses.

Low foetal weights and percentage foetal weights observed in this study, gives credence to reports of low foetal body weights from WAD sheep infected with *T. vivax* (Reynolds and Ekwuruke, 1988; Akinbamijo *et al*., 1994). The trimester of pregnancy and severity of the infection, influenced the weights of the foetuses from the infected-untreated Yankasa and WAD ewes.

Abortions due to the infection were influenced by the trimester of pregnancy, severity of the infection and breed of ewe. Abortions were most common in the Yankasa

than the WAD ewes and in the third trimester than in the first trimester of pregnancy. The abortions observed in the infected-untreated Yankasa and WAD ewes in the third trimester of pregnancy, occurred during the acute phase of the infection when parasitaemia and pyrexia were both high. This showed that Yankasa and WAD ewes foetuses, were most susceptible in the third trimester of pregnancy during the acute phase of infection. Abortions and death of dams early in the infection have been reported in cattle(Ogwu *et al*.,1986). Elhassan (1987), also reported abortions and premature delivery in WAD ewes infected with *T. vivax* in the first and third trimesters of pregnancy.

Stress induced by pyrexia has been reported to activate the production of corticosteroids from the foetal adrenal gland(Tilton *et al*.,1972). These corticosteroids stimulate the production of prostaglandin F2 alpha(PGF2x) and oestrogen from the placenta. The PGF2x initiates abortion by reducing myometrial activity thresh hold, through reduction in concentration of progesterone, while oestrogen causes uterine contraction and expulsion of the foetus (Osborn and Kenedy, 1981; Liggins *et al*.,1972). Direct invasion of the embryo as a result of intra-uterine infections of trypanosomes have been reported (Ikede and Losos, 1972; Nuru, 1974; Ogwu and Nuru, 1981; Ogwu *et al*., 1984; 1986; Elhassan, 1987). These might have contributed to the abortions observed in the Yankasa and WAD ewes in this study.

The effects of the infection on foetuses was influenced by the severity of the infection at each trimester of pregnancy and breed of ewe. Partial foetal resorption(Plate 4.2) and almost complete foetal resorption(Plate 4.1) were observed in the infected-untreated Yankasa ewes infected in the first and second trimesters of pregnancy respectively. These findings coincided with the mild and severe nature of the infections in the Yankasa ewes in the first and second trimester respectively. The fact that these findings

were not observed in the WAD ewes, despite the similar nature of infection in the two breeds in the first and second trimester. Strongly suggest that the WAD ewes tolerated the effects of *T. vivax* infection on foetuses than the Yankasa.

None of the infected-untreated and infected-treated Yankasa in the first, second and third trimester groups carried the pregnancy to term. The infected-untreated WAD ewes in the three trimester groups similarly did not carry their pregnancies to term just as the infected-untreated Yankasa ewes. However the infected-treated WAD ewes in the second and third trimester groups, carried their pregnancies to term and had normal deliveries, unlike treated Yankasa ewes. This suggest that the effects of the infection and treatment on pregnancy and delivery was influenced by the breed of the ewes. The delivery of lambs at term by the infected-treated WAD ewes in the second and third trimesters of pregnancy in this study, showed that Novidium$^{(R)}$ chemotherapy of pregnant WAD ewes will completely ameliorate the pathogenic effects of *T. vivax* infection on pregnancy leading to normal delivery. In contrast, Novidium$^{(R)}$ chemotherapy of pregnant Yankasa ewes will only delay abortions, dystocia or death of foetuses in-utero.

It was concluded from the study that trimester of pregnancy and breed of ewes were important in the pathogenicity of *T. vivax* infection on pregnant Yankasa and WAD ewes. Also *T. vivax* infection in pregnant Yankasa ewes of a short duration, was enough to cause irreversible pathology in the dam and foetus, leading to foetal resorption, foetal death in-utero, abortions and dystocia.

It was deduced from this study, that the trypanotolerance of WAD ewes can be augmented by Novidium$^{(R)}$ chemotherapy to eliminate the pathogenic effects of trypanosomosis

on pregnancy and may enhance the productivity of WAD ewes in trypanosomosis endemic areas.

5.0 CHAPTER FIVE

EFFECTS OF NOVIDIUM(R) [HOMIDIUM CHLORIDE] CHEMOTHERAPY ON THE PATHOLOGICAL LESIONS OF *Trypanosoma vivax* INFECTION IN PREGNANT YANKASA AND WEST AFRICAN DWARF (WAD) EWES.

5.1 SUMMARY

The effects of Novidium$^{(N)}$(Homidium chloride) chemotherapy at 1.0mg/kg body weight, on the pathological lesions produced by *Trypanosoma vivax* infection in pregnant Yankasa and West African Dwarf (WAD) ewes, in the first and second trimesters of pregnancy were comparatively studied. Comparative studies between the infected-treated and infected-untreated Yankasa and WAD ewes, in the third trimester was not possible, because 3 out of the six infected Yankasa ewes either aborted or died without aborting before the day of treatment. Three out of the six WAD ewes also aborted before the day of treatment.

Most severe pathological lesions were observed in the infected-untreated Yankasa and WAD ewes in the second trimester than in the first trimester and more often in Yankasa ewes than in the WAD ewes. These included oedema, congestion and red/gray hepatization of the lungs; severe hepatomegaly with yellowish discoloration of the liver; serous atrophy of coronary fats with yellowish discoloration of the fats; bilateral enlargement and congestion of the kidneys; enlargement and congestion of the adrenal and pituitary glands; peri-orbital oedema/peri-orbital oedema and haemorrhage in the foetuses. These were observed the second trimester and in the infected Yankasa ewes only. The trimester of pregnancy, severity of the infection and breed of ewes, influenced the severity of the lesions observed in the ewes and fotuses.

Resolutions of the pathological lesions observed in the infected ewes folowing treatment, severity of the infection, organ involved and breed of ewe. Early and delayed resolution of the gross and microscopic lesions were observed in the infected-treated Yankasa and WAD ewes in the first and second trimesters of pregnancy respectively.

Exceptions were the enlargement of the adrenal glands and the melanin deposits

in the adrenal glands; degeneration of the granulosa cells of the ovaries in the infected Yankasa ewes in the first trimester. In the second trimester, delayed/incomplete resolution of the histopathological lesions, were observed in the infected-treated Yankasa and WAD ewes. These were the foci of necrosis and coagulative necrosis in the adrenal glands; Fibrosis of the ovaries; Fibrosis of the liver; Degeneration of the liver hepatocyte, kidney tubules and glomerular capillaries; Congestion and gray-red hepatization of the lungs and the inflammatory cellular reactions of the cervix, uterus and cardiac muscles. These lesions were observed more often in the infected-treated Yankasa ewes than in the infected-treated WAD ewes. It was concluded from the study that the success of treatment in the resolution of the pathological lesions in the infected ewes, depended on the trimester of pregnancy, severity of the lesions at the time of treatment, organ involved and breed of ewe.

5.2 INTRODUCTION

The gross pathological lesions reported in animal trypanosomosis include anaemia; emaciation; enlargement of lymph nodes; oedema and/or haemorrhages of the lymph nodes; atrophy of lymph nodes in chronic cases; splenomegaly; hepatomegaly; enlargement, dilation and flabbiness of the heart; extensive petechial haemorrhages of serous cavities, particularly the peritoneum and ecchymotic haemorrhages of the endocardium and epicardium in acute cases [Hall, 1977]. Anosa and Isoun (1983), described oedema of the lymph nodes, haemorrhages of the heart, lungs and the gastrointestinal tract in infected sheep. Microscopically, haemosiderosis in the lymph nodes, spleen and liver; congestion and distention of the hepatic sinusoids were also observed.

Lesions observed in the reproductive and endocrine organs of infected animals included atrophy and cystic degeneration of the ovaries, decreased number or complete absence of secondary follicles, while tertiary follicles show extensive degeneration of granulosa cells and absence of corpus luteum (Isoun and Anosa, 1974; Ogwu, 1983; Mutayoba *et al.*,1988; Lawani, 1989). Lawani(1989), reported that the lesions in ovaries were irrespective of the duration of the infection.

The ovarian stroma of Red Sokoto goats infected with *T. vivax*, has been reported to be infiltrated by mononuclear cells and proliferation of connective tissues (Lawani, 1989). Extensive fibrosis of the ovarian stroma, pyknosis of follicular cells and infiltration of ovarian stroma with mononuclear cells, decrease in number of primordial and primary follicles and atresia of growing follicles at the tertiary stage resulting in lack of corpora lutea, have also been described in East African goats, chronically infected with *T. congolense* (Mutayoba *et al.*, 1988a). Clinically, the ovarian changes in the goats paralled the cessation of oestrous cycles and significant decline in basal peak progesterone and

oestradiol level(Mutayoba, 1988b,c)

Sparse lymphocytic infiltration of the connective tissue capsule, subcapsular and peri-vascular spaces, foci of necrosis, and areas of coagulative necrosis have been described in the pituitary of goats infected with *T. vivax* (Lawani, 1989). Slight atrophy of the pituitary gland accompanied by partial degranulated basophils, with fewer secretory acini and slight hypertrophy of the acidophils in the cortical zone of the adenohypophysis, have also been described in goats infected with *T. congolense* (Mutayoba *et al.*, 1988a).

Severe lesions manifested by focal to diffuse gliosis, infiltration of perivascular spaces and meninges by lymphocytes, macrophages, plasma cells and occasional morula cells in the neurohypophysis, oedema, hyperaemia, thrombosis of sinusoids and acute and focal coagulative necrosis of the adenohypophysis have been reported in sheep, goats and horses infected with *T. brucei*. (Losos and Ikede, 1972., Ikede *et al.*, 1973 Ikede and Losos, 1972, 1975). Severe damage to the pituitary may result in reduced production of gonadotrophins and this may lead to gonadal dysfunction and reduced gonadotrophin support which could explain the degenerative changes in the ovaries(Jeffcoate and Holmes, 1997).

Gross enlargement of the adrenal glands were reported in *T. vivax* infected goats and sheep (Elhassan, 1987; Lawani, 1989). Histopathologically, melanin deposits in capsule, hypertrophy of adrenal cortex and coagulative necrosis in zona glomerulosa were reported in *T. vivax*-infected goats (Lawani, 1989). Foci of mononuclear cellular reaction, fatty degeneration of cells of the zona glomerulosa and fasciculata have been reported in *T. brucei* -infected sheep (Ikede and Losos, 1975). Foci of necrosis in zona fasciculata have also been reported in *T. congolense* infected goats (Mutayoba, *et al.*, 1988a).

Hypertrophy of the adrenal cortex is a common phenomenon in conditions of

stress(Ikede and Losos, 1975), such as observed in infections. This may cause the elaboration of excessive amounts of both mineralocorticoids and glucocorticoids and may result in upset in sodium/potassium balances and in the metabolism of fats and carbohydrates(Lawani, 1989). In pregnant animals excessive amounts of steroids from the foetal adrenals may precipitate expulsion of the foetus.

Lymphocytic infiltrations and oedema of the longitudinal muscles of the cervix have been described in goats infected with *T. vivax* (Lawani, 1989). Similarly, cellular infiltration of cervix, which had non-secretary desquamated mucosa, have been described in Zebu heifers infected with *T. congolense* (Ogwu and Njoku, 1991). The severity of the lesions observed in the heifers was reported to be directly related to the duration of the infection (Ogwu and Njoku, 1991). The inflammatory reactions of the cervix could probably be an attempt by the immune system to combat trypanosome antigens as reported in *T. brucei*-infected rabbits(Van den Ingh and Van Dijk, 1975). An inflamed uterus may also become hostile to the embryo or developing foetus, with attempts to expel it(Hafez, 1968).

Desquamation of vaginal epithelium and accompanied diffused infiltration of the submucosa with lymphocytes, plasma cells, neutrophils, occasional eosinophils and varying degree of perivascular cuffing, have been observed in three goats infected with *T. vivax* (Lawani, 1989). Oedema of the vulva has been reported in *T. vivax*-infected goat (Lawani, 1989), sheep (Elhassan , 1987) and cattle (Ogwu, 1983).

The effects of anti-trypanosomal drug chemotherapy on the pathological lesions due to trypanosomosis in pregnant trypanosusceptible and trypanotolerant breeds of sheep in Nigeria have not been reported. The objective of this study was to comparatively study the effects of Novidium[(n)] (Homidium chloride) chemotherapy at 1.0mg/kg. body weight at 14

days pi. On the pathological lesions in the dams and foetuses, following *T. vivax* infection of Yankasa and WAD ewes in the first and second trimesters of pregnancy.

5.3 MATERIALS AND METHODS

The materials and methods are as described in chapter 4.

Gross and Histopathological studies.

A pair of infected-untreated and infected-treated Yankasa and WAD ewes were sacrificed at 21 days pi and at the end of each trimester period. They were thoroughly examined at ante-mortem and at post-mortem for gross physical and pathological changes. The gravid uteri, foetuses, adrenal and pituitary glands of the ewes, were weighed and recorded for each ewe.

Tissues sections measuring 2.5-3.0mm in thickness were taken from the following organs of each of the ewes sacrificed. Prescapular lymph nodes, liver, spleen, kidneys, uterus, foetal membranes, cervix, and adrenal glands. The pituitary gland and ovaries were preserved whole. The tissues were preserved in freshly prepared 10% buffered formol-saline and in bouins solution in plastic containers, labelled and sent to the histopathology section of the faculty of Veterinary Medicine, Ahamdu Bello University Zaria for processing into slides. The fixed histopathology sections were cut into sections of not more than 2.0mm, then processed as described by Drury *et al*.,(1976), using an automatic Shandon 2L processor MK.11, tissue processor. The tissues were processed in the following order.

1.50% Alcohol	1 hour
2.70% Alcohol	1 hour
3. 90% Alcohol	1 1/2 hours
4. Absolute Alcohol 11	40 minutes
5. Absolute Alcohol 111	2 hours
6. Xylene 1	40 minutes

7. Xylene	11	40 minutes
8. Wax bath	1	1 1/2 hours
9. Wax bath	11	1 1/2 hours

10. Wax bath 111 in vacuum oven for 1 hour.

11. The blocks were then embedded in molten paraffin wax of melting point 54-56oC, allowed to harden at room temperature, and then refrigerated until sectioned.

The Leitz rotary microtome was used to section the tissues to sections of 4-6um thick. The tissues were stained with haematoxylin and eosin (H&E) stain. The tissues were mounted on the microscope slides using Canada balsam. The slides were examine using a Leitz research microscope under oil immersion lens.

6.4 RESULTS

Tables 5.1 and 5.2 are summaries of the gross pathological lesions observed in the infected-untreated and infected-treated Yankasa and WAD ewes and the foetuses.

Pathological findings in the DAM:-

Heart:- Gross lesions.

In the first trimester group, hydropericardium(15.0 ml of fluid) was observed in the infected-untreated Yankasa ewes sacrificed at 21 days pi. Resolution of the lesion was observed in the infected-treated Yankasa sacrificed at 21 days pi. The infected-untreated and infected-treated WAD ewes sacrificed at 21 and 28 days pi, had no hydropericardium (Table 5.1).

Flabbiness of the heart was observed in the infected-untreated Yankasa ewe in the first trimester sacrificed at 21 days pi, while enlargement, dilation and flabbiness of the heart was observed in the infected-untreated Yankasa sacrificed at 28 days pi and in the infected-untreated WAD ewe sacrificed at 21 days pi.

Resolution of the lesions were observed in the infected-treated Yankasa ewes sacrificed at 21 and 28 days pi and in the infected-treated WAD ewe at 21 days pi. The infected-untreated and infected-treated WAD ewes sacrificed at 28 days pi, did not exhibit lesions.

Table 5.1. Gross pathological findings in pregnant Yankasas and WAD ewes in their first trimester of pregnancy, experimentally infected with *Trypanosoma vivax*.

ORGAN/PATHOLOGY	YANKASA		WAD	
	UNTREATED	TREATED	UNTREATED	TREATED
SEROUS CAVITIES				
Atrophy of fats.	NO	No	No	No
Severe atrophy of fats.	No	No	No	N o
LUNGS				
Mild oedema.	-	Yes[21]	No	No
Oedema/congestion	Yes[21]	No	No	No
Oedema,congestion, red/gray hepatization.	No	No	No	N o
HEART				
Hydropericardium.	Yes[21]	No	No	No
Serous atrophy of fats.	No	No	No	No
Severe serous atrophy of fats.	No	No	No	No
Enlargement, dilation and Flabbiness.	Yes[28]	No	Yes[21]	N o
Flabbiness only	Yes[21]	No	No	No
LIVER				
Mild hepatomegaly.	Yes[21]	No	No	No
Severe hepatomegaly.	Yes[28]	No	No	No
Hepatomegaly with yellowish discoloration.	No	No	No	No
SPLEEN				
Splenomegaly.	-	Yes[21]	No	No
Splenomegaly with petechiae haemorrhage.	Yes[21	No	No	No
Severe Splenomegaly.	-	-	Yes[28]	No
Severe Splenomegaly with petechiae haemorrhages.	Yes[28]	No	No	No
Petechiae haemorrhage on normal spleen.	No	No	No	Yes[28]
KIDNEYS				
Enlargement.	Yes[28	No	No	N o
Enlargement and Congestion.	No	No	No	No
Normal but pale kidney	No	No	No	No
LYMPH NODES				
Enlargement and oedema.	Yes[21]	No	No	No
Enlargement, Oedema and haemorrhages.	Yes[28]	No	Yes[28]	No

UTERUS				
Retarded development.	Yes[21,28]	No	No	No
VAGINA				
Haemorrhages.	Yes[21]	No	No	No
INTESTINES				
Haemorrhages.	Yes[21]	No	No	No
PITUITARY				
Enlargement.	Yes[21]	No	No	No
Enlargement and Congestion.	No	No	No	No
ANDRENAL GLANDS				
Enlargement.	-	Yes[28]	Yes[28]	No
Enlargement/Congestion.	Yes[21,28]	-	-	-
FOETUSES				
Retarded development.	Yes[21]	No	No	No
Periorbital oedema.	No	No	No	No

Figures in superscripts are days pi, when the pathology was observed
No = normal organ.

Table 5.2. Gross pathological findings in pregnant Yankasa and WAD ewes in their second trimester of pregnancy, experimentally infected with *Trypanosoma vivax*.

ORGAN/PATHOLOGY	YANKASA		WAD	
	UNTREATED	TREATED	UNTREATED	TREATED
SEROUS CAVITIES				
Atrophy of fats.	Yes[21]	NO	Yes[21,49]	No
Severe atrophy of fats.	Yes[49]	No	No	No
LUNGS				
Mild oedema	-	-	No	Yes[21]
Oedema/congestion.	No	NO	No	No
Oedema,congestion, red/gray hepatization.	No	Yes[49]	No	No
HEART				
Hydropericardium.	No	No	No	No
Serous atrophy of fats.	Yes[21]	No	Yes[21,49]	No
Severe serous atrophy of fats.	Yes[49]	No	No	No
Enlargement, dilation and Flabbiness.	Yes[21,49]	No	Yes[21,49]	No
LIVER				
Hepatomegaly.	Yes[21]	No	Yes[21]	No
Severe hepatomegaly.	-	No	Yes[28]	No
Hepatomegaly with yellowish discoloration.	Yes[49]	No	No	No
SPLEEN				
Splenomegaly.	-	-	-	-
Splenomegaly with petechiae haemorrhage.	No	No	No	No
Severe Splenomegaly.	Yes[21,49]	No	Yes[21]	No
Petechiae haemorrhage on normal spleen.	No	No	No	No
KIDNEYS				
Enlargement.	Yes[21]	No	No	No
Enlargement and Congestion.	Yes[49]	No	No	No
Normal but pale kidney	No	No	Yes[49]	No
LYMPH NODES				
Enlargement and oedema.	No	No	No	No
Enlargement, Oedema and haemorrhages.	Yes[21]	Yes[21]	Yes[21,49]	Yes[21]
Atrophy.	Yes[49]	No	No	No
UTERUS				
Retarded development.	Yes[21,49]	No[21,49]	No[21]Yes[49]	No

VAGINA				
Haemorrhages.	No	No	No	No
INTESTINES				
Haemorrhages.	No	No	No	No
PITUITARY				
Enlargement.	Yes[21]	No	No	No
Enlargement and congestion	Yes[49]	No	No	No
ANDRENAL GLANDS				
Enlargement.	-	Yes[21]	No	No
Enlargement/Congestion.	Yes[21,49]	No[49]	No	No
FOETUSES				
Retarded development.	Yes[21,49]	No	Yes[49]	No
Periorbital oedema.	Yes[21]	Yes[21]	No	No
Periorbital oedema and haemorrhage	Yes[49]	No	No	No

Figures in superscripts are days pi, when the pathology was observed
No = normal organ.

In the second trimester group, enlargement, dilation, flabbiness of the heart with serous atrophy of coronary fats, were observed in the infected-untreated Yankasa ewes sacrificed at 21 days pi and in the infected-untreated WAD ewes sacrificed at 21 and 49 days pi. The infected-untreated Yankasa sacrificed at 49 days pi, had severe serous atrophy of the coronary fats. Resolution of the gross pathological changes were observed in both the infected-treated Yankasa and WAD ewes sacrificed at 21 and 49 days pi(Table 5.2).

Microscopic lesions: In the first trimester group, inflammatory cellular reactions and oedema of cardiac muscle fibers were observed in the infected-untreated Yankasa ewes sacrificed at 21 and 28 days pi and in the infected-untreated WAD sacrificed at 21 days pi(Plate 5.1).

Resolution of the inflammatory cellular reactions were observed in the infected-treated Yankasa ewes sacrificed at 21 and 28 days pi and in the WAD ewe sacrificed at 21 days pi, except for the separation of the cardiac muscles (Plate 5.2). The infected-untreated and infected-treated WAD ewes sacrificed at 28 days Pi, had histopathologically normal hearts. In the second trimester group, inflammatory cellular reactions and oedema of cardiac muscle fibers, were observed in the infected-untreated Yankasa ewe sacrificed at 49 days pi [Plate 5.3], which were not completely ameliorated in the infected-treated Yankasa ewes at 49 days pi.[Plate 5.4].

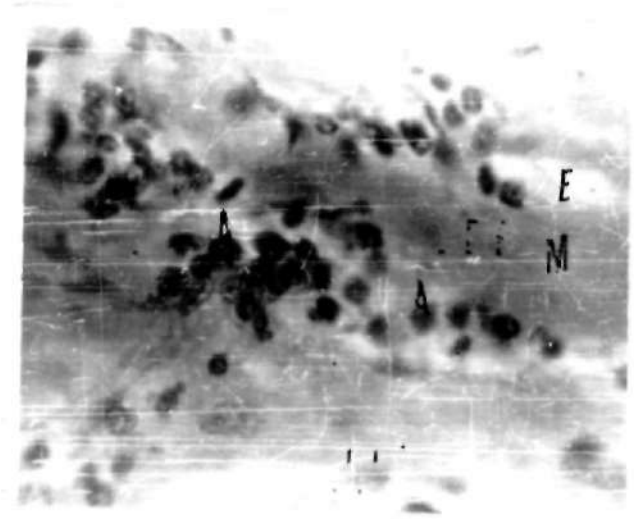


Plate 5.1 Cross section of the heart of *T. vivax* infected-untreated Yankasa ewe (053) in first trimester group, sacrificed at 21 days pi, showing oedema [E] of cardiac muscles [M] and mononuclear cellular infiltrations [A] X 400.

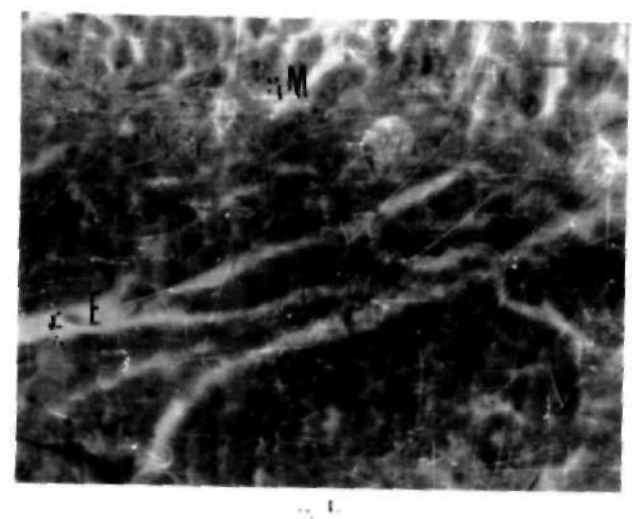


Plate 5.2 Longitudinal section of the heart of *T. vivax* infected-treated Yankasa ewe (0548) in first trimester group, sacrificed at 21 days pi, showing seperation of cardiac muscle[M] due to previous oedematous condition[E],no mononuclear cellular infiltrations X 400.

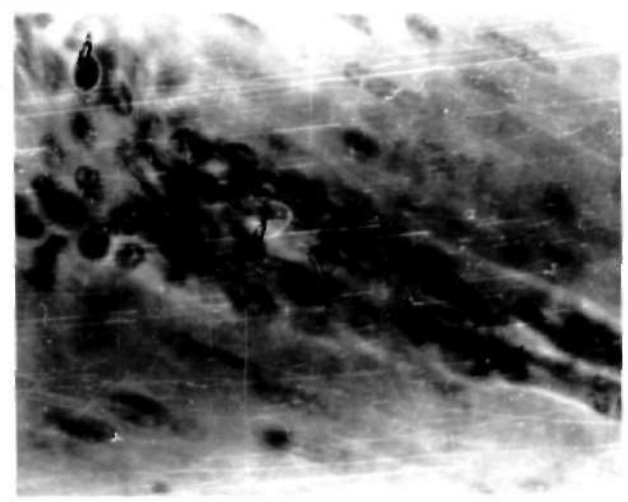


Plate 5.3 Longitudinal section of the heart of *T. vivax* infected-untreated Yankasa ewe (0555) in second trimester group, sacrificed at 49 days pi, showing mononuclear cellular infiltration [A] X 200.

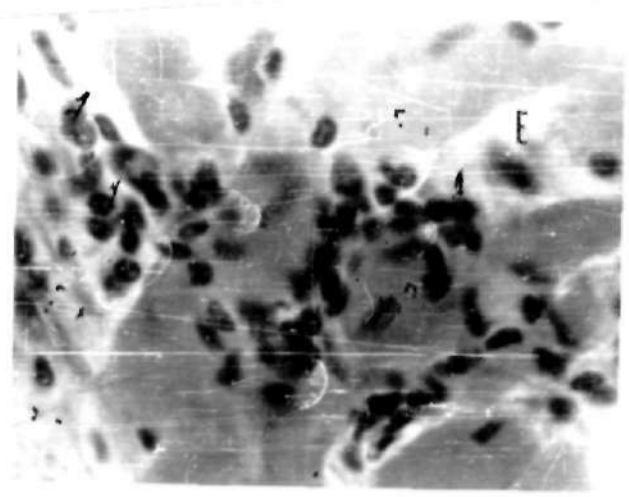


Plate 5.4 Cross section of the heart of *T. vivax* infected-treated Yankasa ewe (1377) in second trimester group, sacrificed at 49 days pi, showing few mononuclear cellular infiltration [A] of the muscle, and oedema [E] of the cardiac muscles X 400.

Oedema of myocardial fibers without inflammatory cellular reactions were observed in both the infected-untreated and infected-treated WAD ewes in the second trimester sacrificed at 49 days pi(Plate 5.5).

Lungs:- Gross lesions

In the first trimester group, congestion and oedema of the lungs were observed in the infected-untreated Yankasa ewe sacrificed at 21 days pi, which was not completely ameliorated in the infected-treated ewe sacrificed at 21 days pi. The infected-untreated and infected-treated Yankasa ewes sacrificed at 28 days pi had normal lungs. Similarly the infected-untreated and infected-treated WAD ewes sacrificed at 21 and 28 days pi, had normal lungs(Table 5.1).

In the second trimester group, mild oedema of the lungs, was observed in the infected-treated WAD ewe sacrificed at 21 days pi, while congestion, oedema and emphysema of the lungs with gray-red hepatization of the lungs was observed in the infected-treated Yankasa sacrificed at 49 days pi(Table 5.2).

Microscopic lesions: Dilated bronchioles and alveoli and massive mononuclear cellular infiltrations in the inter-alveolar septa, were observed in the lungs of the infected-treated Yankasa sacrificed at 21 and 49 days pi.

Liver:-Gross lesions

In the first trimester group, mild and severe hepatomegaly were observed in the infected-untreated Yankasa ewes sacrificed at 21 and 28 days pi, respectively. The lesions were all ameliorated in the infected-treated Yankasa ewes sacrificed at 21 and 28 days pi(Table 5.1). Hepatomegaly was not observed in both the infected-untreated and infected-treated WAD ewes sacrificed at 21 and 28 days pi.

In the second trimester group, hepatomegaly was observed in the infected-untreated

Yankasa ewe sacrificed at 21 days pi, while severe hepatomegaly and yellowish discoloration of the liver(fatty change) was observed in the infected-untreated Yankasa ewe sacrificed at 49 days pi. These were all ameliorated in the infected-treated Yankasa ewes sacrificed at 21 and 49 days pi(Table 5.2). The liver of the infected-untreated Yankasa ewe sacrificed at 49 days pi, was severely enlarged, yellowish and brittle(severe fatty change/necrosis) (Plate 5.6).

Mild hepatomegaly was observed in the infected-untreated WAD ewe in the second trimester sacrificed at 21 days pi. The infected-treated WAD ewe sacrificed at 21 days pi and all the infected-untreated and infected-treated WAD ewes sacrificed at 49 days pi, had grossly normal livers.

Microscopic lesions: Degeneration and replacement of the liver hepatocytes with fat globules(fatty infiltration)and fluid filled necrotic foci, were observed in the liver of the infected-untreated Yankasa ewe in the second trimester sacrificed at 49 days pi(Plate 5.7). The liver of the infected-treated Yankasa ewe sacrificed at 49 days pi, showed degeneration and fibrosis in the portal triad area and necrotic(Plate 5.8).

Inflammatory cellular reactions were observed in the portal triad area, of the liver of the infected-untreated Yankasa and WAD ewes sacrificed at 21 days pi and the infected-untreated WAD ewe sacrificed at 49 days pi. These were all ameliorated in the similar pairs of infected-treated Yankasa and WAD ewes sacrificed at 21 days pi and the infected-treated WAD ewe sacrificed at 49 days pi.

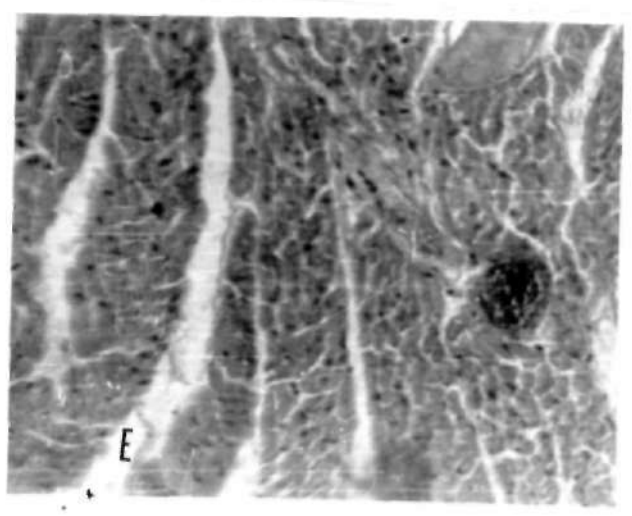


Plate 5.5 Longitudinal section of the heart of *T. vivax* infected-treated WAD ewe (1254) in second trimester group, sacrificed at 49 days pi, showing seperation of muscles due to previous oedematous [E] condition of the cardiac muscles, no mononuclear cellular infiltration. X 400.

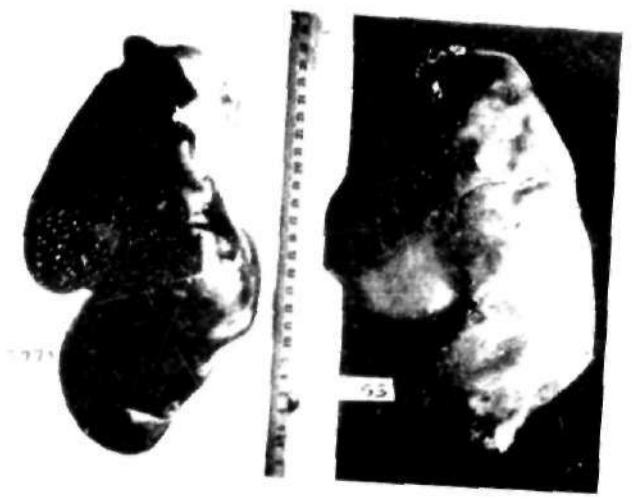


Plate 5.6 Gross picture of livers of infected-treated (1377) and infected-untreated (0555) Yankasa ewes infected with *T. vivax* in second trimester group and sacrificed at 49 days pi, showing very severe hepatomegaly of the liver. The organ was also yellowish and friable.

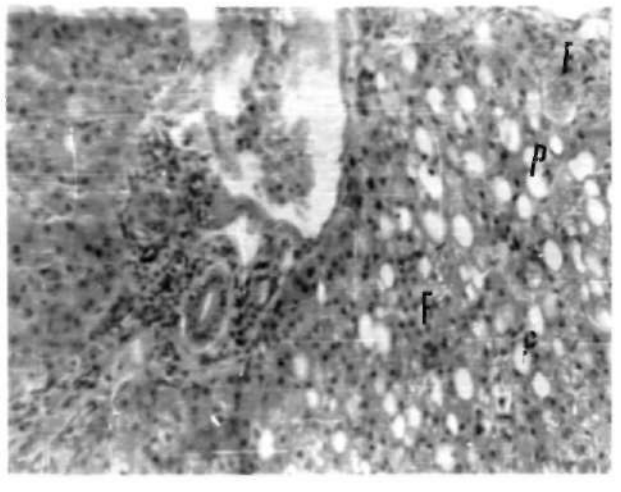


Plate 5.7 Liver of *T. vivax* infected-untreated Yankasa ewe (0555) in second trimester group, sacrificed at 49 days pi showing fatty infiltration [F] and replacement of hepatocyte with adipose fats [P](severe fatty change) x 400.

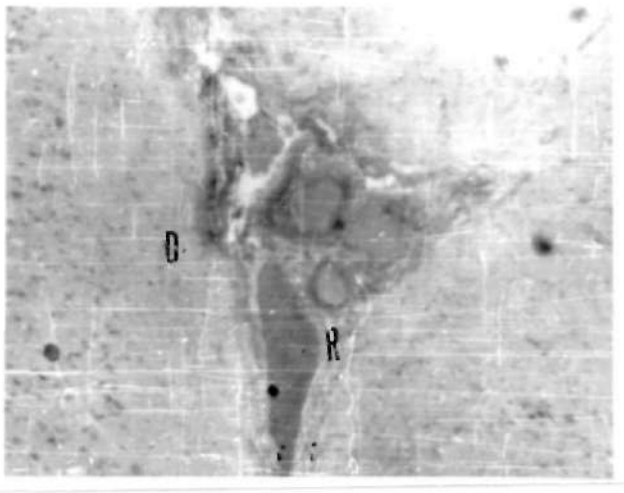


Plate 5.8 Liver of *T. vivax* infected-treated Yankasa ewe (1377) in second trimester group, sacrificed at 49 days pi, showing an area of complete degeneration [D] of liver hepatocyte and fibrosis[R] of the tissue around the hepatic triad x 400.

Spleen:-Gross lesions.

In the first trimester group, splenomegaly with petechial haemorrhages and splenomegaly without petechial haemorrhages were observed in the infected-untreated and infected-treated Yankasa ewes, respectively sacrificed at 21 days, while severe splenomegaly with petechial haemorrhages and severe splenomegaly without petechial haemorrhages were observed in the infected-untreated Yankasa and WAD ewes respectively, sacrificed at 28 days pi. The splenomegaly was completely ameliorated in the infected-treated Yankasa and WAD ewes sacrificed at 28 days pi, except for petechial haemorrhages on the spleen of the WAD ewe sacrificed at 28 days pi(Table 5.1).

In the second trimester group, severe splenomegaly was observed in both the infected-untreated Yankasa and WAD ewes sacrificed at 21 days pi and in the infected-untreated Yankasa sacrificed at 49 days pi. The infected-untreated WAD ewe sacrificed at 49 days pi had a normal spleen. Splenomegaly was not observed in the infected-treated Yankasa and WAD ewes sacrificed at 21 and 49 days pi(Table 5.2).

Microscopic findings: Active and prominent germinal centers were observed in the spleen of the infected-untreated and infected-treated Yankasa and WAD ewes in the first trimester, sacrificed at 21 days pi. Highly active and prominent germinal centers were observed in the infected-untreated Yankasa and WAD ewes in the first trimester, sacrificed at 28 days pi. The infected-treated Yankasa ewe sacrificed at 21 had prominent germinal centers. While the infected-treated WAD ewe sacrificed at 21 dys pi, had histologically normal spleen.

Lymph nodes:- In the first trimester group, enlargement and oedema and severe enlargement, oedema and haemorrhages of the prescapular lymph nodes, were observed in the infected-untreated Yankasa ewe sacrificed at 21 days pi and in the infected-untreated Yankasa and WAD ewes sacrificed at 28 days pi, respectively. These were all ameliorated

in the similar pair of infected-treated Yankasa and WAD ewes(Table 5.1).

In the second trimester group, enlargement, oedema and haemorrhages of the prescapular lymph nodes were observed in both the infected-untreated and infected-treated Yankasa and WAD ewes sacrificed at 21 days pi and in the infected-untreated WAD ewe sacrificed at 49 days pi, while atrophy of the lymph nodes were observed in the infected-untreated Yankasa ewe sacrificed at 49 days pi. The lesions were not ameliorated in the infected-treated Yankasa and WAD ewes sacrificed at 21 days pi, but were ameliorated in the infected-treated Yankasa and WAD ewes sacrificed at 49 days pi(Table 5.2).

Microscopic findings:

Very active germinal centers and thickening of the lymph nodes capsules, were observed in both the infected-untreated Yankasa and WAD ewes in the first and second trimester sacrificed at 21 days pi. The infected-treated Yankasa and WAD ewes in the first and second trimester sacrificed at 21 days pi, had histologically normal lymph nodes.

Foci of necrotic cysts in the capsule of the lymph nodes and depletion of the germinal centers of lymphocytes were observed in the infected-untreated Yankasa and WAD ewes in the first trimester, sacrificed at 28 days pi. The similar pair of infected-treated Yankasa and WAD ewes had histologically normal lymph nodes.

Thickening of the lymph nodes capsules with necrotic cysts in the capsules, were observed in the infected-untreated Yankasa ewes in the second trimester, sacrificed at 49 days pi. Depletion of the lymph nodes corpuscles of lymphocytes and connective tissues infiltration of the medullary and cortical areas of the lymph nodes were also observed in the infected-untreated Yankasa ewe in the second trimester, sacrificed at 49 days pi. The infected-treated Yankasa ewes had connective tissues infiltration of the medullary and cortical areas and depletion of lymph nodes corpuscles of lymphocytes.

Inactive lymphoid corpuscles and depletion of the lymphoid corpuscles of lymphocytes were observed in the infected-untreated WAD ewe in the second trimester sacrificed at 49 days pi. The similar pair of infected-treated WAD ewe had histologically normal lymph nodes.

Kidneys:- Gross lesions.

In the first trimester group, bilateral enlargement of the kidneys was observed in the infected-untreated Yankasa ewe sacrificed at 28 days pi. The lesion was ameliorated in the similar pair of infected-treated Yankasa ewe. The infected-untreated and infected-treated WAD ewes sacrificed at 21 and 28 days pi had normal kidneys(Table 5.1).

In the second trimester group, bilateral enlargement and congestion of the kidneys were observed in the infected-untreated Yankasa ewe sacrificed at 49 days pi. The lesion was ameliorated in the similar pair of infected-treated Yankasa ewe. All the WAD ewes in the first and second trimester groups had normal kidneys(Tables 5.1, 5.2).

Microscopic findings: Inflammation of the kidney tubules was observed in the infected-untreated Yankasa sacrificed at 28 days pi, in the first trimester, while severe inflammation of the kidney tubules and degeneration of the glomerular capillaries leaving empty bowmans capsules, were observed in the kidneys of the infected-untreated Yankasa ewe sacrificed at 49 days pi, in the second trimester [Plate 5.9]. Only inflammation of the kidney tubules and glomerular capillaries was observed in the infected-treated Yankasa ewe sacrificed at 49 days pi(Plate 5.10). The similar pair of infected-treated Yankasa and WAD ewes in the first trimester had histologically normal kidneys.

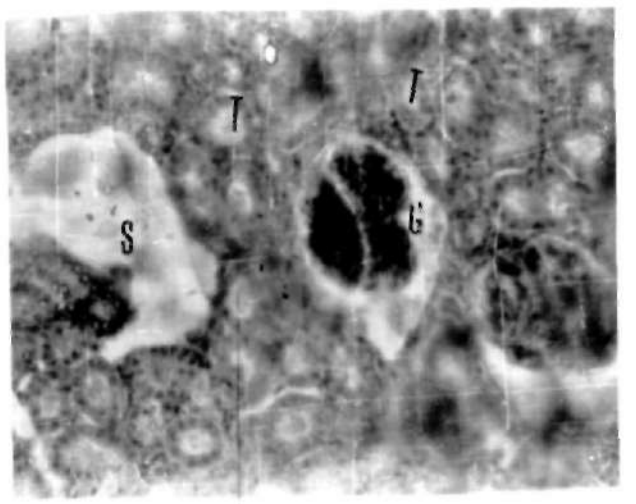


Plate 5.9 Kidney of *T. vivax* infected-untreated Yankasa ewe (0555) in second trimester group, sacrificed at 49 days pi, showing inflammation and degeneration of the kidney tubules[T] and glomerular capillaries[G] of the bowman capsules leaving empty spaces[S] x 400.

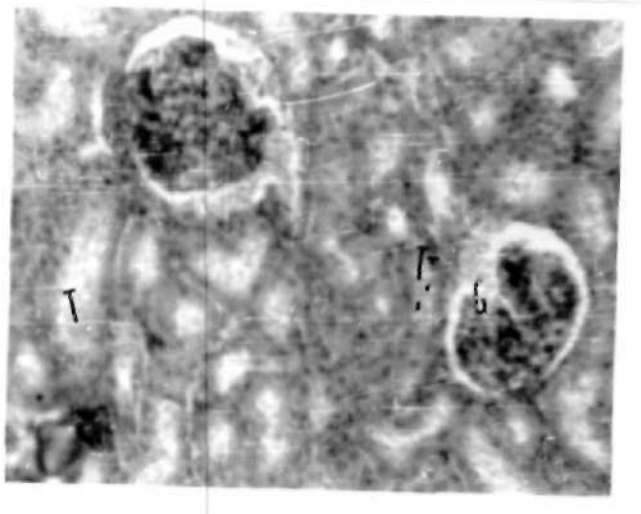


Plate 5.10 Kidney of *T. vivax* infected-treated Yankasa ewe (1377) in second trimester group , sacrificed at 49 days pi, showing severe inflammation of the kidney tubules[T] and glomerular capillaries[G] of the bowman capsules, x 400.

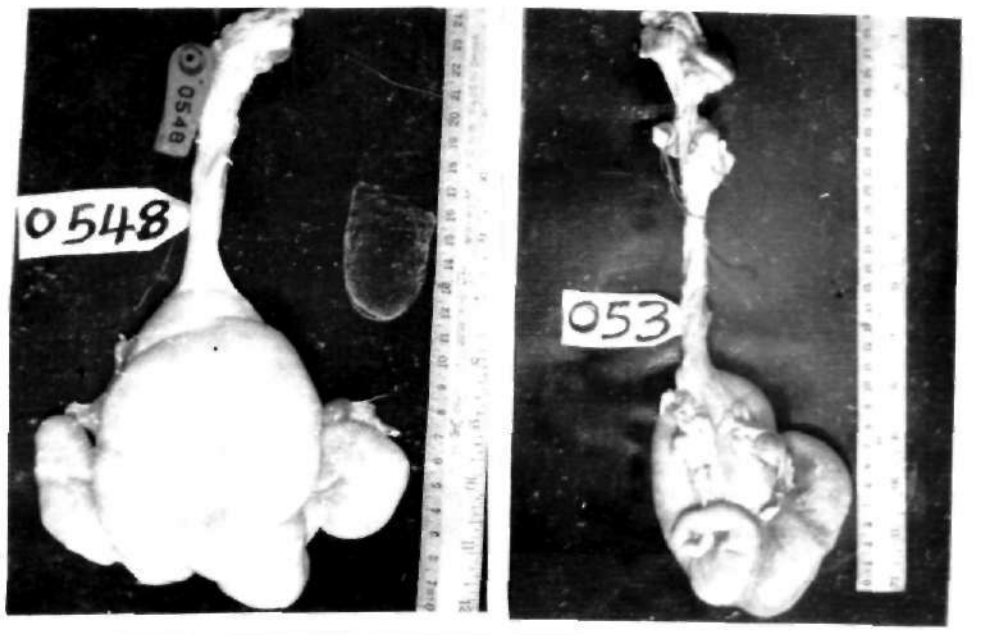


Plate 5.11 Forty four (44) days old gravid uteri of infected- treated (0548) and infected-untreated (053) Yankasa ewes infected with *T. vivax* in first trimester and sacrificed at 21 days pi, showing retarded development of the uterus of the infected-untreated ewe, in contrast to the uterus of the infected-treated ewe.

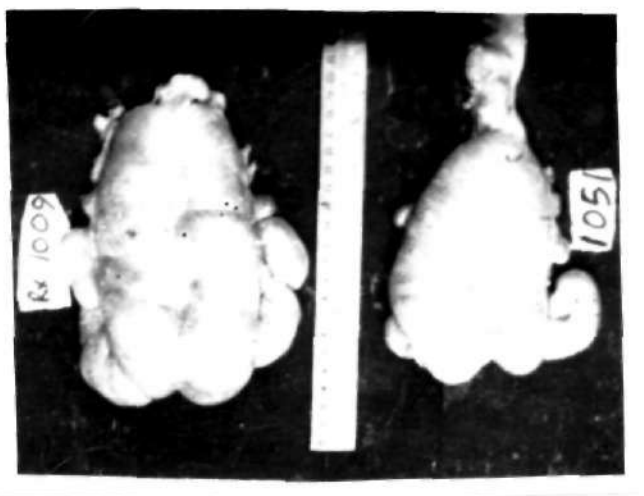


Plate 5.12 Fifty one(51) days pregnant uteri of infected-treated(1009) and infected-untreated (1051) Yankasa ewes infected with *T. vivax* in first trimester and sacrificed at 28 days pi, showing retarded development (smaller in size) of the uterus of the untreated ewe (1051) in contrast to the treated ewe.



Plate 5.13 Sixty-three (63) days Pregnant uterus of and infected-untreated Yankasa ewe infected with *T. vivax* in second trimester, that died acutely from the infection at 11 days pi, showing severe retarded development of the uterus. The uterus is much smaller than uteri from similar Yankasa ewes (Plate 5.8 and 5.9).

UTERUS:-Gross findings.

In the first trimester group, the gravid uteri of the infected-untreated Yankasa ewes sacrificed at 21 and 28 days pi, were smaller in size(retarded development), than the uteri from the similar pair of infected-treated Yankasa ewes[Plates 5.11; 5.12]. The gravid uteri from the infected-untreated and infected-treated WAD ewes in the first trimester were similar in size and weight.

In the second trimester group, the gravid-uteri from the infected-untreated Yankasa ewes sacrificed at 21 and 49 days pi and from the infected-untreated WAD ewe sacrificed at 49 days pi, were smaller in size than the gravid uteri of the similar pair of infected-treated Yankasa and WAD ewes.

Severe retarded uterine development was observed in the infected-untreated Yankasa ewe that died at 11 days pi, at 63 days of pregnancy(Plate 5.13). The uterus was much smaller in size than 44 days old pregnant uterus of an infected-untreated Yankasa ewe in the first trimester[Plate 5.11].

Microscopic findings: In the first trimester group, inflammatory cellular reactions were observed in the wall of the blood vessels of the endometrium, of the infected-untreated Yankasa ewe sacrificed at 21 days pi. The similar pair of infected-treated Yankasa ewe, the infected-untreated and infected-treated WAD ewes sacrificed at 21 days pi, had no histopathological lesions in the uterus.

Inflammatory cellular reactions were observed in the body of the uterus and in the lumina of the glands of the endometrium of the infected-treated Yankasa ewe sacrificed at 28 days pi. In the WAD ewes, inactive non-secretory uterine glands and placenta with foci of necrosis and devoid of placenta villi was observed in the infected-untreated WAD ewe, sacrificed at 28 days pi. The similar pair of infected-treated WAD ewe, had active endometrial glands and inflammatory cellular reactions in endometrium.

In the second trimester group, inflammatory cellular reactions were observed in the uterus in the infected-untreated and infected-treated WAD ewe sacrificed at 21 days pi and in the infected-treated WAD ewe sacrificed at 49 days pi. Massive inflammatory cellular reactions of the endometrium of uterus and necrosis of the placental villi, were observed in the infected-untreated WAD ewe sacrificed at 49 days pi.

CERVIX:-Gross lesions

No gross pathological lesions, were observed in the cervix of both the infected-untreated and infected-treated Yankasa and WAD ewes in the first and second trimesters of pregnancy

Microscopic findings:- In the second trimester group, massive inflammatory cellular infiltration, was observed in the cervix of the infected-untreated Yankasa ewe sacrificed at 49 days pi. [Plate 5.14] The Similar pair of infected-treated Yankasa ewe showed incomplete resolution of the inflammatory cellular reactions [Plate 5.15].

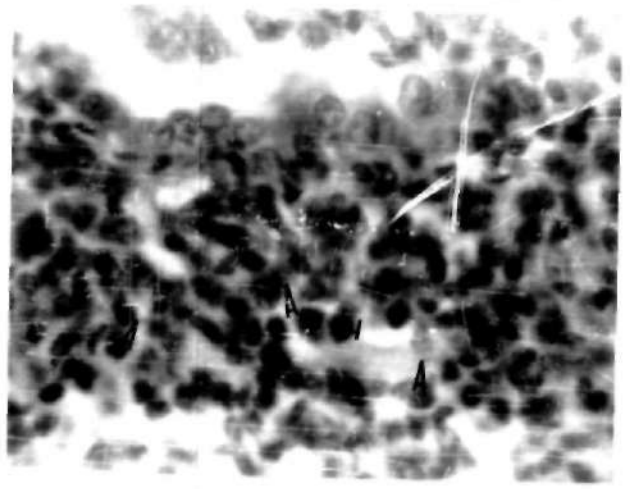


Plate 5.14 Cervix of *T. vivax* infected-untreated Yankasa ewe(0555) in second trimester group, sacrificed at 49 days pi showing massive mononuclear cellular infiltration[A] including giant cells x 400.

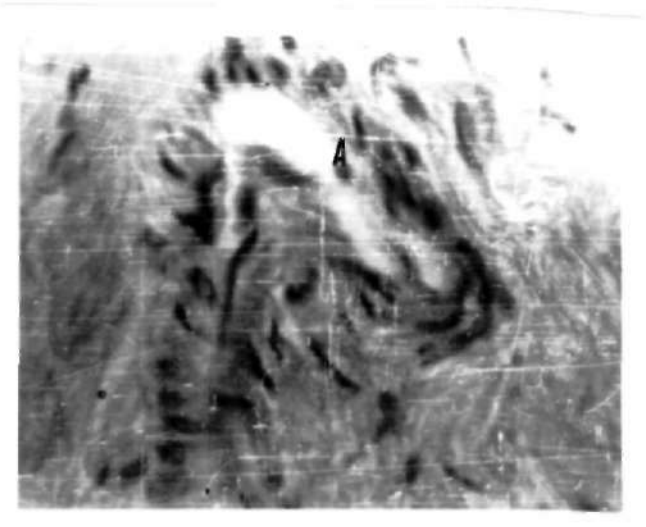


Plate 5.15 Cervix of *T. vivax* infected-treated Yankasa ewe(1377),in second trimester group, sacrificed at 49 days pi, showing few mononuclear cellular infiltrations[A] x 400.

OVARIES:-

In the first trimester group, degenerating primary and tertiary follicles with varying degrees of degenerating granulosa cells were observed in both the infected-untreated and infected-treated Yankasa ewes sacrificed at 28 days pi[Plate 5.16; 5.17; 5.18; 5.19]. In the second trimester group, fibrosis of the ovaries with few to complete absence of primary or tertiary follicles were observed in the infected-untreated Yankasa and WAD ewes sacrificed at 49 days pi(Plate 5.20).

FOETUSES:-

In the first trimester group, the foetus from the infected-untreated Yankasa ewe sacrificed at 21 days pi, was smaller in size and body weight than the foetus from the similar pair of infected-treated ewe.

In the second trimester group, the foetuses from the infected-untreated Yankasa ewes sacrificed at 21 and 49 days pi [Plates 5.21; 5.22] and the foetus from the infected-

untreated WAD ewe sacrificed at 49 days pi. were smaller in size and body weight than the foetuses from the similar pair of infected treated Yankasa and WAD ewes.

Peri-orbital oedema was observed in both the infected-untreated and infected-treated Yankasa ewes foetuses, in the second trimester sacrificed at 21 days pi (Plate 5.21), while very severe peri-orbital oedema and haemorrhage was observed in the foetus from the infected-untreated Yankasa ewe sacrificed at 49 days pi. The peri-orbital oedema was completely ameliorated in the infected-treated Yankasa ewe foetus sacrificed at 49 days pi(Plate 5.22).

Partial resorption of the foetus was observed in the infected-untreated Yankasa ewe in the first trimester, that died at 64 days of pregnancy, that was at 41 days pi, while almost complete resorption of the foetus was observed in the infected-untreated Yankasa ewe, in the second trimester that died from the infection at 11 days pi, that was at 63 days of pregnancy.

ENDOCRINE ORGANS:-

PITUITARY:-Gross lesions.

Enlargement of the pituitary gland was only observed in the infected-untreated Yankasa ewe in the first trimester, sacrificed at 21 days pi. The pituiary gland of the infected-untreated Yankasa ewe sacrificed at 21 days pi, weighed 0.9gms, while that of the infected-treated Yankasa ewe weighed 0.4gms. The enlargement was ameliorated in the infected-treated Yankasa ewes(Table 5.1).

In the second trimester group, enlargement of the pituitary gland was observed in the infected-untreated Yankasa ewe sacrificed at 21 days pi, while enlargement and congestion of the pituitary gland was observed in the infected-untreated Yankasa ewe sacrificed at 49 days pi. The gland weighed 1.02gms. The inflammation was ameliorated

in the infected-treated Yankasa ewes sacrificed at 21 and 49 days pi(Table 5.2). The infected-untreated and infected-treated WAD ewes in the first and second trimester groups, all had grossly normal pituitary glands.

Microscopic findings:-Areas of light staining indistinct acidophils and areas of complete loss of basophils, acidophils and chromaphores were observed in the pituitary of the infected-untreated Yankasa ewe, in the second trimester sacrificed at 49 days pi. Melanin deposits were observed in the pituitary of the infected-untreated WAD in the second trimester sacrificed at 21 days pi.

ADRENAL GLANDS:-Gross lesions

In the first trimester group, enlargement of the right adrenal gland and enlargement and congestion of the left adrenal gland were observed in the Yankasa ewe sacrificed at 28 days pi. The right and left adrenal glands weighed 1.557gms and 2.622 gms respectively. Bilateral enlargement of the adrenal glands was observed in the infected-untreated WAD ewe sacrificed at 28 days pi. The left adrenal gland weighed 1.556 gms, while the right gland weighed 1.602gms.

No gross lesions were observed in both the infected-untreated and infected-treated WAD ewes sacrificed at 21 days pi. The average weight of the glands was 1.29 gms

Complete resolution of the gross lesions of the adrenal glands was observed in the infected-treated Yankasa ewe sacrificed at 21 days pi, and in the infected-treated WAD ewe sacrifieced at 28 days pi, but not in the infected-treated Yankasa ewe sacrificed at 28 days pi(Table 5.1). The adrenal glands of the infected-treated Yankasa ewe sacrificed at 28 days pi, weighed 2.613 gms and 1.92 gms for the left and right adrenal glands, respectively.

In the second trimester group, enlargement / hyperaemia and enlargement/congestion of the adrenal glands, were observed in the infected-untreated and

infected-treated Yankasa ewes sacrificed at 21 days pi, respectively, while enlargement and congestion was observed in the infected-untreated Yankasa ewe sacrificed at 49 days pi. The average weight of the glands was 2.71 gms. The infected-treated Yankasa ewe sacrificed at 49 days pi, had grossly normal glands, with an average weight of 1.40 gms.

Microscopic findings:- foci of necrosis in the medulla and melanin deposits in the zona fasciculata, were observed in the infected-untreated Yankasa ewe sacrificed at 28 days pi, while only melanin deposits in zonal fasciculata were observed in the infected-treated Yankasa ewe sacrificed at 28 days pi. Foci of necrosis in zona fasciculata were observed in the infected-untreated WAD ewe sacrificed at 28 days pi. The infected-treated WAD ewe had no microscopic lesions.

In the second trimester group coagulative necrosis and melanin deposits in zona fasciculata was observed in the adrenal gland of the infected-untreated Yankasa ewe sacrificed, at 21 days pi [Plate 5.23]. The similar pair of infected-treated Yankasa ewe had no lesions. Foci of necrosis in virtually all the layers of the adrenal gland were observed in the infected-untreated Yankasa ewe sacrificed at 49 days pi, while the infected-treated Yankasa ewe sacrificed at 49 days pi, had only few foci of necrosis restricted to the zona fasciculata[Plate 5.24].

Foci of necrosis in zona fasciculata was observed in both the infected-untreated and infected-treated WAD ewes sacrificed at 21 days pi. while foci of necrosis turned cyst (coagulative necrosis) were observed in both the infected-untreated and infected-treated WAD ewes sacrificed at 49 days pi.

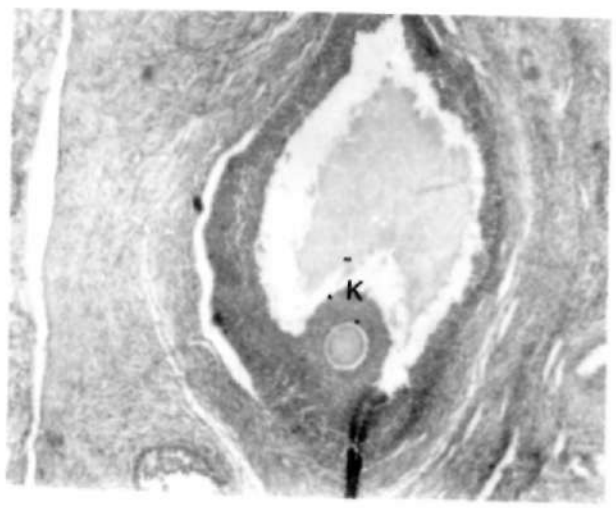


Plate **5**.16 Ovary of *T. vivax* infected-untreated Yankasa ewe (1051) in first trimester group, sacrificed at 28 days pi, showing a matured follicle[K] x 400.

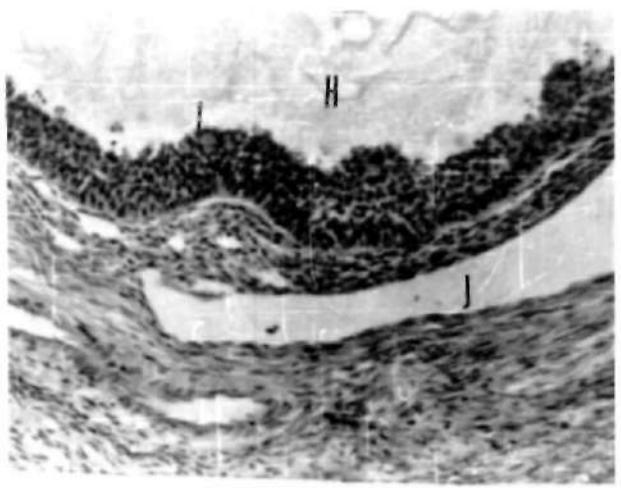


Plate 5.17 Ovary of *T. vivax* infected-untreated Yankasa ewe (1051) in first trimester group, sacrificed at 28 days pi, showing a degenerated follicle[H] and granulosa cells[I] detached from the basement membrane[J] x 400.

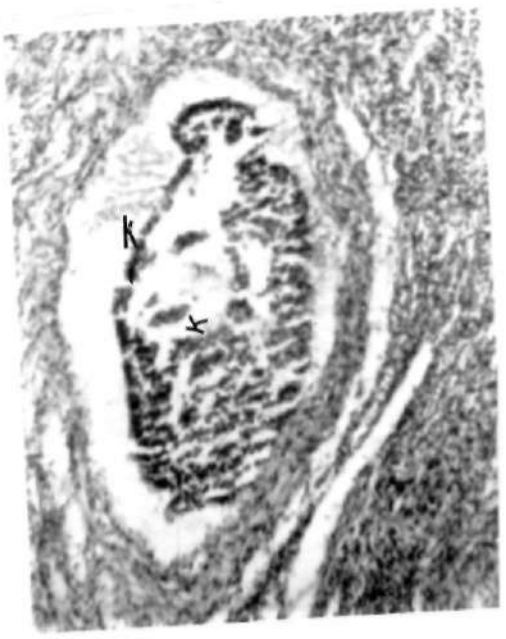


Plate 5.18 Ovary of *T. vivax* infected-treated Yankasa ewe (1009)in first trimester group, sacrificed at 28 days pi showing advanced degeneration of the follicle[K] x 400.



Plate 5.19 Ovary of *T. vivax* infected-treated Yankasa ewe (1009)in first trimester group, sacrificed at 28 days pi, showing a degenerated follicle, degeneration and sloughing of the granulosa cells[I] into the atrium[U] of the follicle x 400.

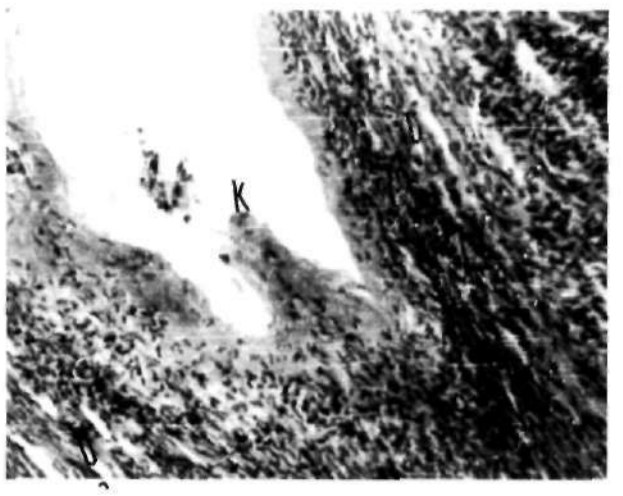


Plate 5.20 Ovary of *T. vivax* infected-treated Yankasa ewe (1377)in second trimester group, sacrificed at 49 days pi, showing fibrosis[O] of the ovary and degeneration of the follicle[K] x 400.

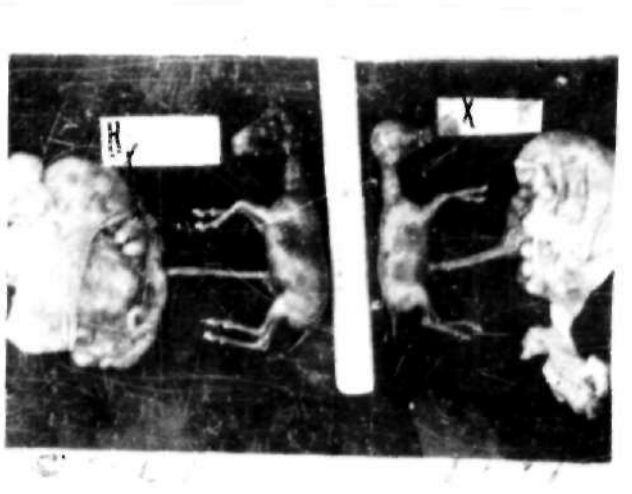
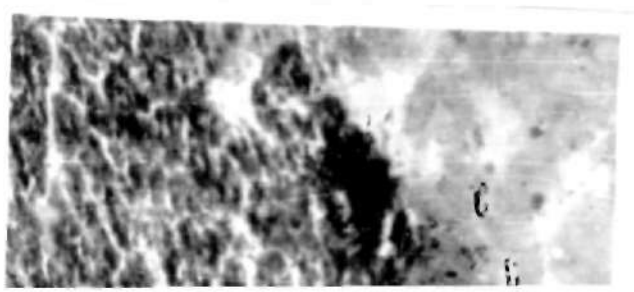


Plate 5.21 Seventy three (73) days old foetuses from *T. vivax* infected-untreated (1051)[X] and infected-treated (0554)[Rx] Yankasa ewes in second trimester group, sacrificed at 21 days pi, showing retardation of foetal growth of the infected-untreated ewe foetus (1051) and periorbital oedema in both foetuses.



Plate 5.22 One hundred and one (101) days old foetuses from *T. vivax* infected-untreated (0555)[X] and infected-treated (1377)[Rx] Yankasa ewes in second trimester group sacrificed at 49 days pi., showing retarded foetal growth and severe peri-orbital oedema and haemorrhage in the infected-untreated ewe foetus (0555), in contrast to the infected-treated ewe foetus(1377).



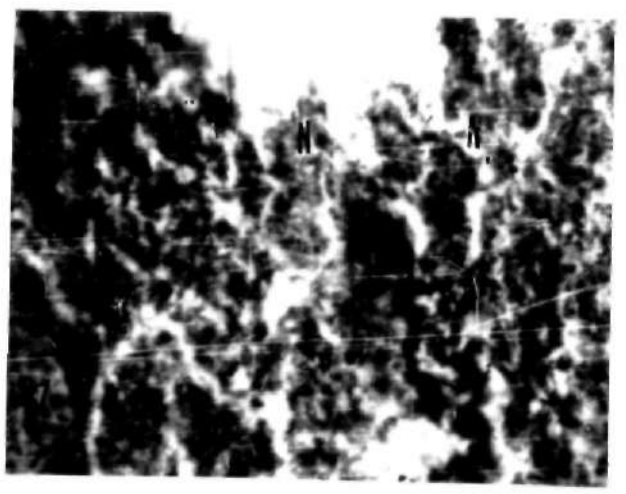


Plate 5.24 Adrenal gland of *T. vivax* infected-treated Yankasa ewe (1377) in second trimester group, sacrificed at 49 days pi(35 days post treatment), showing foci of necrosis[N] in zona fasciculata[Z] of the gland x 400.

6.5 DISCUSSION

The gross and histopathological lesions observed in the infected-untreated Yankasa and WAD ewes in this study were influenced by the severity of the infection, the stage of pregnancy and breed of ewe. The infection was mild in both the Yankasa and WAD ewes in the first trimester and severe in both breeds in the second trimester of pregnancy. Similarly most of the severe gross and histopathological lesions in this study, were observed in the second trimester than in the first trimester. This agrees with the report of Akpavie *et al*.,(1987), that the severity of the lesions in infected ewes, were influenced by the severity of the infection. The lesions were observed more often in the Yankasa ewes than in the WAD ewes. This also showed that WAD ewes tolerated the pathogenic effects of *T. vivax* infection better than the Yankasa ewes.

The gross pathological lesions observed in the infected-untreated Yankasa and WAD ewes in this study, are similar to those that have previously been described (Hall, 1977; Vickerman and Barry, 1982; Anosa and Isoun, 1983; Ogwu *et al*., (1986; Lawani, 1989; Blood and Radostitts, 1990).

The oedema, emphysema and red/gray hepatization observed in the lungs of the infected-treated Yankasa ewe in the second trimester but not in the similar pair of infected-untreated Yankasa ewe, is probably because in this study the ewes with the most severe clinical signs were selected for treatment.

The inflammatory cellular reactions, oedema observed in the cardiac muscles of both the infected-untreated Yankasa and WAD ewes in the first and second trimesters of pregnancy, gives credence to reports by Bungener and Mehlitz (1977), that *T. vivax* invades solid tissues particularly the heart causing extensive inflammatory reactions. The resultant oedema and extravasation of parasites and leucocytes may among other effects

cause separation of the myocardial fibers. Vascular disturbances and disruption of tissue architecture most importantly in the heart and brain have also been reported to be common in animal trypanosomosis (Vickerman and Barry, 1982).

The oedema, congestion with or without red/gray hepatization, observed on the infected-untreated Yankasa ewes in this study, might have been caused by damage to blood vessels by the trypanosomes. Damage to blood vessels which may lead to fibrinous exudation into the Lungs, have been reported in *T. vivax* infected animals (Masake, 1980; Anosa, 1983).

The severe degeneration of the kidneys and capillaries in the bowmans capsule and leaving empty bowman capsules as observed in the infected-untreated Yankasa ewe in the second trimester, can be attributed to immune-complex deposits in the renal tubules. Immune-complex deposits have been demonstrated in the renal glomeruli of animals infected with trypanosomosis (Murray, 1974, Nagle *et al.*, 1974). These immune-complexes are reported to be liable to phagocytosis (Goodwin, 1971, Losos and Ikede , 1972). During the latter process, there may be leakages of enzymes from the macrophages into the surrounding tissues, which might be cytolytic to the tissue cells (Morrison *et al.*, 1978).

The peri-orbital oedema in the foetuses of infected-untreated and infected-treated Yankasa ewes at 28 days pi and the severe peri-orbital oedema and haemorrhage in the foetus of the infected-untreated-Yankasa ewe at 49 days pi, were observed both in the second trimester. None was observed in the foetuses in the first trimester group. This showed that the severity of the lesions in the foetuses was also influence by trimester of pregnancy and severity of the infection.

Peri-orbital oedema in foetuses perhaps have not been reported earlier than now,

however, Ikede and Losos (1975) reported that blindness may result from too much pressure due to fluid accumulation in the chambers of eyes of sheep infected with *T. congolense*.

Severe cases of low foetal weights observed in this study, were observed in the infected-untreated Yankasa ewes foetuses in the second trimester. A case of almost complete foetal resorption was also observed in one infected-untreated Yankasa ewe foetus in the second trimester. The only case of low foetal weight in the WAD ewes foetuses was also observed in the second trimester. This showed that the effects of the infection on foetuses was influenced by the trimester of pregnancy, severity of the infection and breed of ewe.

The microscopic ovarian lesions observed in this study, were more severe in the second trimester than in the first trimester and were characterized by degenerating primary and tertiary follicles in the first trimester and ovarian fibrosis in the second trimester. This finding gives credence to observations by Mutayoba *et al*., (1988a) in goats infected with *T. vivax*, The latter reported that the development of ovarian lesions and dysfunction was directly related to the severity of the infection in the individual goats.

The occurrence of ovarian lesions in the Yankasa ewes and not in the WAD ewes in the first trimester, despite the similar nature of the infection in both breeds in this trimester, is indicative of breed effect. The various ovarian lesions observed in both the infected-untreated and infected treated Yankasa and WAD ewes in this study have been reported in *T. vivax* infected red Sokoto goats (Lawani, 1989); *T. congolense* infected goats (Mutayoba *et al*., 1988a); *T. vivax* and *T. congolense* infected Zebu heifers (Ogwu *et al*., 1984; Ogwu and Njoku, 1991). The significance of the ovarian lesions in this study, is that the sensitivity of the ovaries to gonadotrophin may be reduced (Jeffcoate and Holmes,

1997). Ovarian lesions in female goats infected with *T. congolense* have also been described to parallel the cessation of oestrous cycles and significant decline in plasma progesterone and oestradiol levels (Luckins *et al.*,1986; Mutayoba *et al.*,1988 b,c).

The cervicitis observed in the infected-untreated and infected-treated Yankasa in the second trimester sacrificed at 49 days pi, have been reported in infected-untreated Red Sokoto does infected with *T. vivax* (Lawani, 1989) and in Zebu heifers infected with *T. congolense (*Ogwu and Njoku, 1991). Similarly the inflammatory cellular reactions observed in this study, have been reported in Zebu heifers infected with *T. vivax* (Ogwu, 1983). The significance of the cervicitis and the inflammatory cellular reactions in the uterus, is that the inflammatory reactions might have contributed to the abortions and foetal resorption observed in the ewes in this study, by making the uterine environment hostile to the foetus thereby leading to its expulsion by the uterus or death and resorption.

The gross lesions observed in the adrenal glands in the ewes in this study, have been reported. Lawani (1989), reported slight enlargement of the adrenal glands of Red Sokoto goats infected with *T. vivax*, while Elhassan (1987), observed enlarged adrenal glands in 1 out of 5 pregnant WAD ewes infected with *T. vivax*. Similarly the foci of necrosis and melanin deposits in zona fasciculata, foci of necrosis turned cyst (coagulative necrosis) in zona glomerulosa, observed in this study have also been reported in Red Sokoto goats (Lawani, 1989). The foci of coagulative necrosis and melanin deposits in zona fasciculata, observed in the infected-untreated ewe in the second trimester have not been reported. Foci of necrosis in zona fasciculata have however been reported in goats(Mutayoba *et al.*, 1988a).

The light staining indistinct acidophils and areas of complete loss of acidophils, basophils and chromaphores observed in the infected-untreated Yankasa ewes in the

second trimester group, agree with reports of Mutayoba *et al*., (1988a), in goats infected with *T. vivax* The resolutions of gross and histopathological lesions in the dam in this study were influenced by the severity of the infection at the time of treatment, organ involved and breed of ewe. In the first trimester group, in which the clinical manifestation of the infection was mild, early resolution of the gross pathological lesions was achieved in the infected-treated Yankasa and WAD ewes within 14 days post treatment(28 days pi). Exceptions are the gross lesions observed in the adrenal glands of the Yankasa ewes. Early resolution of histopathological lesions were also observed in both the infected-treated Yankasa and WAD ewes within 14 days post-treatment(28 days pi). Exceptions are the lesions in the adrenal glands, ovaries and oedema of the cardiac muscles, observed only in the infected-treated Yankasa ewes.

In the second trimester group, in which the clinical manifestation of the infection was severe, complete resolution of gross lesions was achieved in both the infected-treated Yankasa and WAD ewes by 35 days post treatment(49 days pi). Except the gross lesions observed in the lungs of the infected-treated Yankasa ewes. Incomplete/non resolution of the microscopic lesions within 35 days post treatment, were observed in liver, kidneys, cervix, uterus and lungs of the infected-treated Yankasa ewes and in the ovaries, adrenal and cardiac muscles of both infected-treated Yankasa and WAD ewes. The incomplete to non-resolution of gross and microscopic lesions in some of the organs of the Yankasa and WAD ewes in the second trimester, showed that the severity of the infection influenced the effects of Novidium$^{(R)}$ chemotherapy on the resolution of the histopathological lesions. This also showed that Novidium$^{(R)}$ chemotherapy and ellimination of trypanosomes in the infected ewes, is probably not enough for complete resolution of lesions in organs such as lungs, liver, kidneys, adrenal glands, cervix, uterus and ovaries within 35 days of treatment.

The incomplete / non-resolution of microscopic lesions in some of the organs in the second trimester, showed that the severity of the infection vis as vis the lesions at the time of treatment, influenced the success of treatment in the resolution of the lesions and gives credence to previous reports(Ikede and Akpavie, 1982). They reported that the severity of lesions at the time of treatment appeared to be more important than the duration of lesions before treatment and regeneration of the affected tissues, depended on the severity of the initial lesions. The organ involved also influenced the success of treatment in the resolution of the lesions.

It was concluded from the study that the severity of the gross and histopathological lesions in the infected ewes and their foetuses was influenced by the severity of the infection and breed of ewe. The success of treatment in the resolution of both the gross and histopathological lesions were influenced by the severity of the lesions, organ involved and breed of ewes.

6.0 CHAPTER SIX

GENERAL DISCUSSION

It was established from the present study, that both Yankasa and West African Dwarf ewes, will develop clinical trypanosomosis similar to those reported by other workers (Losos, 1978; Ogwu and Njoku, 1987; Bawa *et al*., 1990). Individual variations in susceptibility occur in both breeds, similar to previous observations in trypanosusceptible and trypanotolerant cattle (Desowitz, 1959; Margaret *et al*., 1988).

The study showed that the clinical manifestation of the infection in both breeds is influenced by the trimester of pregnancy, ewes in advanced pregnancy are more susceptible. Yankasa ewes in the third trimester of pregnancy may develop a more severe form of the disease and die due to the infection. This observation gives credence to similar observations in pregnant Zebu heifers (Ogwu and Njoku, 1987). The present study also showed that Yankasa and WAD ewes in the first trimester of pregnancy tolerated the infection better than the ewes in the second and third trimester groups. The stage of Pregnancy therefore influenced the susceptibility of the ewes to the infection.

It was observed that WAD ewes tolerated the anaemia due to *T. vivax* infection better than the Yankasa, even when the infection is both severe in the Yankasa and WAD ewes. Anaemia is the most significant clinical feature of trypanosomosis(Fiennes, 1970; Losos and Ikede, 1972; Murray, 1978; Murray and Morrison, 1978, 1981) and survival of infected animals is directly related to the level of parasitaemia and severity of anaemia. Murray (1987), attributed the ability to resist anaemia as an attribute of tolerance to trypanosomosis. The ability of the WAD ewes in this study to control anaemia, therefore

showed that the WAD ewes have attributes of tolerance to the pathogenic effects of *T. vivax* infection. This also explained the differences observed between the Yankasa and WAD ewes in this study, with regards to the effects of the infection on abortions, death of ewes, decline in body weights, low weights of foetuses, pregnancy/delivery and the pathological lesions in the dam and foetuses.

Abortions due to the infection were observed in the infected Yankasa ewes in the three trimesters of pregnancy and in the infected WAD ewes in the second and third trimesters of pregnancy. These were ameliorated in the infected WAD ewes by Novidium(R) chemotherapy at 1.0mg/kg body weight. The infected-treated WAD ewes also carried the pregnancies to term and had normal delivery, in contrast to the infected-treated Yankasa. Death due to the infection was also observed in the infected-untreated Yankasa ewes in the three trimester groups, but was only observed in one WAD ewe in the second trimester group. Similarly significant ($P<0.05$) differences in body weights changes, were observed between the Yankasa and WAD ewes in all the three stages of pregnancy. These findings further confirm that the WAD ewes exhibited some tolerance to the pathogenic effects of *T. vivax* infection. Self cure from the infection was also possible in the WAD ewes.

Partial and almost complete foetal resorption, were only observed in the Yankasa ewes. Similarly low foetal weights were commonly observed in the Yankasa ewes, but only observed in one infected-untreated WAD ewe foetus in the second trimester. This showed that foetuses from Yankasa ewes were more susceptible to the pathogenic effects of *T. vivax* infection than WAD those of ewes.

The infected-untreated Yankasa and WAD ewes and the infected-treated Yankasa in the three trimester groups, did not carry the pregnancies to term. The foetuses died and were either resorbed, aborted or expelled autolyzed. In contrast, the infected-treated WAD

ewes carried their pregnancies to term and had normal deliveries. This finding showed that, *T. vivax* infection in pregnant Yankasa ewes and in infected-untreated WAD ewes, will result in various detrimental effects on pregnancy which may lead to foetal death and resorption, foetal death in-utero and expulsion of dead autolyzed foetuses, abortions or dystocia, which may not be ameliorated by Novidium$^{(R)}$ chemotherapy.

Early resolutions of both the gross and histopathological lesions in the dam and the foetuses, depended on the trimester of pregnancy, severity of the lesions at the time of treatment, organ involved and breed of ewe. Early resolutions of the pathological lesions were observed in the infected-treated Yankasa and WAD ewes in first trimester of pregnancy, the trimester in which the infection was mild. In the second trimester groups, in which the infection was severe in both breeds than in the first trimester group, delayed to non-resolution of some of the gross and histopathological lesions were observed in both the Yankasa and WAD ewes. These findings give credence to the report of Ikede and Akpavie(1982), that the success of chemotherapy in resolution of pathological lesions was influenced by the severity of the infection and lesions at the time of treatment. The present study also showed that the success of Novidium$^{(R)}$ chemotherapy in the resolution of histopathological lesions in pregnant Yankasa and WAD ewes was influenced by the organ involved. Severe lesions of the adrenal glands, heart, cervix and ovaries, may not be ameliorated by chemotherapy within a period of 35 days of treatment.

It was concluded from this study the stage of pregnancy influences the susceptibility of pregnant Yankasa and WAD ewes to *T. vivax* infection. The severity of the infection increases as pregnancy advanced. Pregnant Yankasa ewes in the third trimester were most susceptible to the infection. However WAD ewes will tolerate *T. vivax* infection and also limit the pathogenic effects of the infection on anaemia, body weight changes, weight of

foetuses, pregnancy/delivery and death of ewes, better than the Yankasa ewes. Self cure from the infection was possible in the WAD ewes infected in the first trimester. Individual variations in susceptibility however exist in both breeds.

Chemotherapy was generally more beneficial in limiting the infection, enhancing the early recovery from clinical, haematological, reproductive, hormonal and other pathological organ damages in the WAD ewes than in the Yankasa.

From this study, it is shown that WAD ewes exhibit tolerance to *T. vivax* infection and that the trypanotolerance of WAD ewes can be augumented with Novidium(R) chemotherapy, to improve their productivity in areas endemic in trypanosomosis.

REFERENCES

Abebe,G. and Eley, R.M. (1992a). Trypanosome-induced hypothyroidism in cattle. *British Veterinary Journal 148:63-70.*

Abebe, G. and Eley, R.M. (1992b). Hypothalamic-pituitary adrenal axis responsiveness to insulin-induced hypoglycaemia is modified by trypanosome infection in Boran cattle. *Research in Veterinary Science 53,68-73.*

Abebe, G. Shaw, M.K. and Eley, R.M. (1993a).*Trypanosoma congolense* in the microvasculature of the pituitary gland of experimentally infected Boran cattle. *Veterinary Pathology 30,401-409.*

Abebe, G. Eley, R.M. and Ole-Moiyoi. O.K. (1993b). Reduced responsiveness of the hypthalamic-pituitary-adrenal axis in Boran cattle infected with *Trypanosoma congolense. Acta Endocrinologica 129, 75-80.*

Abou-Ela, A; Askalany, M.A.E; Ragab, A.M., Rashad S; Gad-EL-Maula, B.L.(1987).Variations of gonadotrophins in male camels naturally infected with *Trypanosoma evansi*, before and after treatment. *Veterinary Medicine Journal. (Giza) 34: 356 - 373.*

Ademosun, A.A.(1985). Contribution of Research Small Ruminants Production in Nigeria. *In proceedings:- National Conference on Small Ruminants Production in Nigeria, NAPRI Zaria Oct. 6th - 10th 1995. P.8-34.*

Adenowo, T.K. (1989). Effects of Experimental *Trypanosoma vivax*, infection on the estrous cycle of mature Yankasa ewes. *MSc. Thesis Ahmadu Bello University Zaria Nigeria. p.156.*

Adeyemo, O., Oyejide, A. and Agbedana, O. (1990). Plasma testosterone in *T. congolense* and *T. brucei*-infected West African dwarf rams. *Animal Reproduction Science 22, 21-26.*

Adu, I.F., (1972). The Influence of two systems of Management on the age at Puberty of Nigerian Dwarf Sheep. *BSc. Dissertation, University of Ibadan, Nigeria.*

Adu, I.F. (1980). Investing in Nigerias future with sheep and goat production. *West African Farming, Food and Processing, May 1980. p16-18.*

Adu, I.F., Ngere, L.O. (1979). The Indigenous Sheep of Nigeria. *World Review of Animal Production Vol. XV No.3 p 51-61.*

Agu, W.E. (1983). Animal trypanosomiasis in Nigeria ACIAR. *Proceedings series no. 4: 50 -60.*

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Akinbamijo, O.O., Reynolds, L. and Gort, G. (1994). Effects of *Trypanosoma vivax*, infection during pregnancy, on feed intake, nitrogen retention and live weight changes in West African Dwarf ewes. *Journal of Agricultural Science 123 (3): 379 - 383.*

Akol, G.W.O., Murray, M. (1981). Early events in the pathogenesis of African trypanosomiasis in cattle, localised skin reactions (chancre) which follows the bites of *Glosina morsitans* infected with *Trypanosoma congolense; Trypanosoma brucei*, and *Trypanosoma vivax. Proceedings 17th Meeting of the International Scientific council, Arusha Tanzania October 1981 P. 230 - 233.*

Akpavie, S.O.; Ikede, B.O; Egbunike, G.N., (1987). Ejaculate characteristics of sheep infected with *Trypanosoma brucie* and *Trypanosoma vivax*; Changes caused by treatment with diminazene aceturate. *Research in Veterinary Science. 42: 1- 6.*

Amole, B.O. Clarkson, A.B. and Shear, M.L (1982). The Pathogenesis of anaemia in *Trypanosoma brucei*-infected mice. *Infection and Immunity 36: 1060 -1068.*

Anene B.M., Chime A.B.; Anika, S.M (1991). The productive performance of imported Friesian cattle under heavy Trypanosoma challenge in a rain forest zone of Nigeria. *British Veterinary Journal 147: 275 - 282.*

Anosa, V.O.(1983). Diseases produced by *Trypanosoma vivax* in horses and rodents. *Zentrablatt Fur Veterinamedizin.1983 717-741.*

Anosa, V.O. (1988). Haematological and biochemical changes in human and animal trypanosomiasis Part 1. *Revue D'elevage et de Medecine Ve'te'rinaire des Pays Tropicaux. 1988; 41: 65 - 78.*

Anosa,V.O. and Isoun, T.T. (1974). Experimental *Trypanosoma vivax* infection of sheep and goats:- The relationship between parasitaemia, the growth rate and anaemia. *Journal of Nigerian Veterinary Medical Association. 3: 102 - 108.*

Anosa,V.O. and Isoun,T.T.(1976). Serum proteins, blood and plasma volumes in experimental *Trypananosoma vivax* infections of sheep and goats. *Tropical Animal Health and Production Journal. 8:14-19.*

Anosa, V.O. and Isoun, T.T. (1980). Haematological studies of *Trypanosoma vivax* infection of goats and intact and splenectomized sheep. *Journal of Comparative Pathology 90: 155 - 188*

Anosa, V.O. and Isoun,T.T.(1983). Pathology of experimental *Trypanosoma vivax* infection of sheep and goats. *Zentralblatt Veterinamedizin Reihe. B 30; 685 - 700.*

Anosa, V.O. and Kaneko, J.T. (1984). The Pathogenesis of *Trypanosoma brucei*, infection in deer mice (*Peromyscus maniculatus)*. iii. Light and electron microscopic study of testicular pathology. *Veterinary Pathology. 21:238-246.*

Apted, F.I.C. (1970) The African typanosomes. Eds. H.W. Mulligan and W.H. Potts. London George Allen and Urwin. p661 - 683.

Ashcroft, M.T. (1959). The importance of African wild animals as reservoirs of trypanosomiasis. *East African Medical Journal. 36: 269 (abstr.).*

Assoku, R.K.G. (1975) Immunological Studies of the mechanism of anaemia in experimental *Trypanosoma evansi* infection in rats. *International Journal for Parasitology 5: 137- 145.*

Asuamah, K.Y. (1977) Nomadism and cattle production in Nigeria" Proceedinds. *First continuing Education course for Veterinarians. Ed. O.O. Akerejola and Y.O. Aliu PP. 275- 283.*

Bambino, T.H. and Tsuch, A.J.W.(1981). Direct inhibitory effect of glucorcorticoids on LH receptors and steroidogenesis in vivo and in vitro. *Endocrinology, 108: 2142-148.*

Bangham, A.D. and Blumberg, B.S. (1958). Distribution of electrophoretically different haemoglobins among some cattle breeds of Europe and Africa. *Nature, (London)181:1551-1552.*

Banks, K.L. (1978). The binding of *Trypanosoma congolense*, to the walls of small blood vessels. *Journal of Protozoology 25:241 - 245.*

Barry, J.D and Hajduk, S.L. (1979).Antigenic heterogeneity of blood stream and metacyclic forms of *Trypanosoma brucei; In. Lossos, G. and Chouinard, A. (eds). Pathogenicity of trypanosomes. p.51 IDrc Ottawa, Canada.*

Barry, J.D. Hajduk, S.L. Vickerman, K and Le-Ray, D. (1979). Detection of multiple variable antigen types in metacyclic populations of *Trypanosoma brucei; Transactions of the Royal Society for Tropical Medicine and Hygiene 73: 205.*

Bawa, E.K., Oyedipe, E.O., Sannusi A.; Eduvie, L.O. Ogwu D; Esievo, K.A.N (1990). Effects of *Trypanosoma vivax* infection on-pregnancy in Yankasa and West African Dwarf sheep:- comparative clinical observation between Yankasa and WAD sheep, following infection at second and third trimester of pregnancy. *NAPRI- ABU Zaria (1990) Bulletin p.87 - 89.*

Blood, D. C; Radostitts, O. M.(1990), Diseases caused by trypanosomes. *In Veterinary Medicine v11th Edition ELBS, Bailiere Tindall. p1013.*

Boch, J; Weiland, T. Bachtaler E; Geisselbrecht R.h; Meinrich H.D; Willberge G; Reiter L.(1984).Parasitological, clinical and serological findings in Dahomey cattle experimentally infected with *Trypanosoma conglense* and *Trypanosoma brucei. Berlin Und Munch Tier Woch. 97: 398 - 404.*

Boreham P.F.L and Facer C.A. (1973). Fibrinogen degradation products of African trypanosomiasis. *Transactions of the Royal society for Tropical Medcine and Hygiene 67; 279 abstract.*

Boycott, A. E., Price-Jonnes, C.(1913). Experimental trypanosome anaemia. *Journal of Pathology and Bacteriology 17:347-366.*

Bungener,W and Mehlitz, Z.(1977). Extravascular localization of *Trypanosoma vivax* in cattle. *Tropenmedizin Und Parasitologie. 28:8-10.*

Bungener W. and Muller, G. (1976). Adherence phenomena in *Trypanosoma conglense.*Tropenmedizin *und Parasitologie 27: 270 - 383.*

Boyt, W.T. (1971). Trypanosomiasis control in Rhodesia. *Bullettin International Journal of Epizootics. 76: 301 - 306.*

Chandler, R.L. (1952). Comparative tolerance of West African N'dama cattle to trypanosomiasis *Annals of Tropical Medicine and Parasitology. 46:127-134.*

Capbern, A., Giroud, C., Baltz, T. and Mattern, P. (1977). Trypanosoma equiperdum. Etude des variations antigeniques au cours de la trypanosomes experimentale du Lapin. *Experimental Parasitology. 42: 6-13.*

Clarkson, M.J. (1968). Blood and plasma volumes in sheep infected with *Trypanosoma vivax. Journal of comparative pathology 78:189-193.*

Clarkson, M.L., Penhale, W.J., Edwards, G.,Farnel, P.F(1975). Serum protein changes in cattle infected with *Trypanosoma vivax. Transactions of the Royal Society of Tropical Medicine and Hygiene. 69:2 abstract.*

Coulomb, J.,Gruvet, J., Morel, P.C.,Perreau, P., Queval, R., Tibayrene, R and Provost, A.(1978). Trypanotolerance, bibliographical synthesis of present knowledge. *Report of the Institut d'elevage et de medicine Veterinaire des pays tropicaux Maisons Alfort, France.*

Crowe, J.S., Barry, J.D., Hajduk, S.L. and Vickerman, (1981).Monoclonal antibodies against variable antigen types of metacyclic *Trypanosoma brucei. Transactions of the Royal Society for Tropical Medicine and Hygeine 75: 894.*

Cunningham, M.P. and Vickerman, K. (1962). Antigenic analysis in the *Trypanosoma brucei* group, using the haemagglutination reaction. *Transactions of the Royal Society for Tropical Medicine and Hygiene 56: 48-60.*

Dargie, J.D. (1978). Erythrocyte response in bovine trypanosomiasis In. Pathogenicity of Trypanosomes. *Proceedings of a Workshop held at Nairobi Kenya. Ed. Lossos, G and Chouinard, A. 128 - 134.*

Dargie, J.D., Murray, P.K., Murray, M. Goimshaw W.R.T. and McIntyre, W.I.M. (1979a). Bovine Trypaanosomiasis:- The red cell kinetics of Ndama and Zebu cattle infected with *Trypanosoma congolense. Parasitology, 78: 271 - 286.*

Dargie, J.D, Murray, P.K, Murray M, McIntyre W.I.M (1979b).The blood volumes and erythrokinetics of Ndama and Zebu cattle, exterimentally infected with *Trypanosoma brucei.Research in Veterinary Science 26:245-244.*

David West, K.B. (1985). Role of government in small ruminants production. *Proceedings of the National Confernce on Small Ruminants Production, NAPRI, Zaria p10 - 17.*

Desowitz, R.S. (1959). Studies on immunity and host-parasite relationsips. 1-The immunological response of resistant and susceptible breeds of cattle to trypanosomal challenge. *Annals of Tropical Medicine and Parasitology. 53: 293 - 313.*

Diggs, C., Flemming, B., Dillon, J., Snodgrass R., Campbell, G. and Esser, K. (1976). Immune-serum mediated cytotoxicity against *Trypanosoma rhodesiense. Journal of Immunology, 116, 1005-1011.*

Djabakou, K., Fimmen, H.O. , Karbe, E. (1981). Natural infection of *Trypanosoma vivax* in trypanotolerant cattle. *17th Meeting International Scientific council for Trypanosomiasis research and control Arusha, Tanzania, P 337 - 342.*

Doyle, J.J., Hirumi, H., Hirumi, K. Lupton, E.N. and Cross, G.A.M.(1980). Antigenic variation in clones of animal-infective *Trypanosoma brucei* derived and maintained in vitro. *Parasitology 80: 359.*

Drury, R.A.B. and Wallington, E.A. (1987). *In Carletons Histology Techniques. 4th Edition, Oxford University Press, London, 33-99.*

Duncan, M. Mwange., William, K. Munyua and P.N.Nyaga (1990). Immunosuppression in caprine trypanosomiasis: Effects of acute Trypanosoma congolense infection on antibody response to Anthrax spore vaccine. *Tropical Animal Health and Production Journal. 22: 95-100.*

Edeghere, H; Igweh, A.C. and Falope, O.O. (1986). Comparative study of experimental *Trypanosoma brucei, brucei; Trypanosoma congolense* and *Trypanosoma vivax* infections in Yankasa rams. *Paper presented at the 11th Annual Conference of the Nigerian Society for Animal Production, Faculty of Veterinary Medicine Ahmadu Bello University Zaria, 23rd to 27th March 1986.*

Edeghere, H., Elhassan, E., Abenga, J., Osoe, H.O., Lawani, F.A.G. and Falope O. (1992) Effects of infection of *Trypanosoma brucei* at different trimesters of pregnancy in ewes.*Veterinary Parasitology. 43:203-209.*

Eduvie, L. O.(1985). Factors affecting Post-partum Ovarian activity and Uterine involution in Zebu cattle indigenous to Nigeria. *Animal Reproduction Science. 8: 123 - 128.*

Edwards, E.E., Judd, J.M. and Squire, F.A.(1956).Observations of trypanosomiasis of domestic animals in West Africa. 1.The study index of infection and weekly haematological values in goats and sheep infected with *Trypanosoma vivax, Trypanosoma congolense* and *Trypanosoma brucei. Annals of Tropical Medicine and Parasitology 50: 223 - 241.*

Elhassan, E.O. (1987). Pathophysiology of female reproduction in sheep experimentally infected with *Trypanosoma vivax. PhD. Thesis, University of Ibadan, Ibadan Nigeria.*

Elhassan, E., Ikede, B.O., Adeyemo O. (1991). Commencement of cyclicity in suckling ewes infected with *Trypanosoma vivax. Abstr. Incl. OAU/STRC 1991: 15 No. 7082, 511.Tsetse and Trypanosomiasis imformation News, March 1992 p.34.*

Emery, D.L., Akol. G.W.O., Murray, M., Marrison, W.I. and Mollo, S.K. (1980a). The chancre - early events in the pathogeniesis of African trypanosomiasis in domestic Livestock. In. Van Den Bossche, H. (ed). The host-invader interplay. *Proceedings of the third International, Symposium on the Biochemistry of Parasites and Host-Parasite Relationship P. 345. Elsevier/North Holland Biomedical Press, Amsterdam.*

Emery, D.L., Barry J.D. and Moloo S.K. (1980b). The appearance of Trypanosoma (Duttonella) vivax in Lymph, following challenge of goats with infected *Glossina morsitans, morsitans. Acta tropica. 37: 375.*

Emery, D.L. and Moloo, S.K. (1981). The dynamics of the cellular relations elicited in the skin of goats by *Glossina morsitans, morsitans.* infected with *Trypanosoma vivax. Acta Tropica in Press (cited from Vickerman and Barry, 1982 Immunology of Parasitic infections 2nd Ed. Eds, Cohen and Warren K, Oxford Press P. 204 - 260.*

Esievo. K.A.N. (1979). In vitro production of neuramidase [Sialidase] by *Trypanosoma vivax. Proceedings of the 16th meeting of the OAU/STRC International Council for trypanosomiasis research and control Yaounde, Cameroon. Oct., 29- Nov. 3 p. 205-210.*

Esievo, K.A.N. (1980). Studies on an aspect of anaemia of bovine trypanosomiasis (*Trypanosoma vivax*). *PhD. Thesis A.B.U. Zaria, Nigeria.*

Esievo, K.A.N., Moore, W.E., Muller R. (1982). Scanning electron microscopy of erythrocytes from *Trypanosoma vivax* infected cattle. Department of Laboratory Medicine and Pathology, Kansas state University. Manhattan U.S.A [unpublished].cited from Esievo and Saror(1991). Immunochemistry and Immunopathology of Animal Trypanosomiasis. *Protozoological Abstracts Vol 15(7): 337-349.*

Esievo, K.A.N. and Saror, D.I. (1983). Leucocyte response in experimental *Trypanosoma vivax* infection in cattle. *Journal of comparative Pathology 93: 165 - 169.*

Esievo, K.A.N., Sarror D.I. (1991). Immunochemistry and Immunopathology of Animal Trypanosomiasis. *Protozoological Abstracts Vol 15(7): 337-349.*

F.A.O. 1982. Production year book, 32. Rome Italy.

Facer, C.A., Cross key, J.M., Clarkson, M.J. and Jenkins, G.C.(1982).Immune haemolytic anaemia in bovine trypanosomiasis. *Journal of Comparative Pathology 92: 393 - 401.*

Fiennes, R.N.T.W. (1954). Haematological studies in trypanosomiasis of cattle. *Veterinary Record. 66: 423-434.*

Fiennes, R.N.T.W. (1970). Pathogenesis and Pathology of animal Trypanosomiasis: *In: the African trypanosomes,Mulligan, H.W. and Potts, W.H. Ed. G. Unwin Ltd London 729-750.*

Fio - Ngaindiro, G. (1987). Development of animal industry and improvement of animal health in the Central African Republic. *Rev. Sci. et. Techn. 6: 955 - 967.*

Francis, D.A. (1988) Livestock and Farming Systems in South-West Nigeria. In Smith, O.B. and Bosman, H.G (Eds). Goat Production in the humid tropics. *Proceedings of Workshop at University of Ife, Ile-Ife, Nigeria, 20-24th July 1987. Pudoc. Wageningen, 1988 Pp 159-169.*

Glover, P.E. (1961).The tsetse problem in Northern Nigeria" *Pasture News Agency (E.A) Ltd, Nairobi Kenya P. 383.*

Godfrey, D.G., Killick - kendrick, R. and Ferguson, W. (1964). Bovine trypanosomiasis in Nigeria III - A high incidence in a group of West African humpless Cattle *"Annals of Tropical Medicine and Parasitology. 58: 204 - 215.*

Goodwin, L.G (1970). The pathology of African Trypanosomiasis. *Transactions of the Royal Society for Tropical Medicine and Hygiene 64:797-812.*

Goodwin, L.G. and Guy, M.W. (1973) "Tissue fluids in rabbits infected with *Trypanosoma brucei. Parasitology. 66:499-513.*

Goodwin, L.G. (1974). The African Scene: Mechanisms of Pathogenesis in trypanosomiasis "In. *Elliot, K., O'Connor, M. and Wolsten Holme, G. E. W. (Eds). Trypanosomiasis and Leismaniasis with special reference to chaga's Disease. Ciba Foundation Symposium. No. 20 (New Services). Amsterdam Association of Scientific Publishers 107-119.*

Gray, A.R. (1965). Antigenic variation in a strain of Trypanosoma brucei transmitted by Glossina morsitans and Glosinna palpalis. *Journal of General Microbiology 41: 195.*

Gray, A.R. (1975. A Pattern in the development of agglutinogenic antigens of cyclically transmitted isolates of *T. gambiense. Transactions of the Royal Society for Tropical Medicine and Hygiene. 69: 131-138.*

Griffin, L. (1978). African Animal trypanosomiasis in sheep and goats. *A review. Veterinary Bullettin. 48: 819 -825.*

Griffin, L. (1983). Congenital transmission of Trypanosoma conglense. in mice. *Journal of Comparative Pathology. 93: 489 - 492.*

Griffin, L. and Allonby, E.W. (1979a). Studies on the epidemiology of trypanosomiasis in sheep and goats at a range research station in Kenya. *Tropical Animal Health and Production 11: 133 - 142.*

Griffin, L. and Allonby, E.W. (1979b). Trypanotolerance in breed of sheep and goats with an experimental infection of Trypanosoma conglense. *Veterinary Parasitology 5: 97-105.*

Griffin L. and Allonby, E.W. (1979c). Disease syndrome in sheep and goats naturally infected with Trypanosoma congolense. *Journal of Comparative Pathology. 89: 457 - 465.*

Hadjuk, S.L., Cameron, C.R., Barry, J.D. and Vickerman, K. (1981). Antigenic Variation in cyclical transmitted *Trypanosoma brucei.* variable antigen type composition of metacyclic trypanosomes population from the salivary glands of glossina morsitans. *Parasitology 83. 595.*

Hafez, E.S.E.(1968). Environmental effects on Animal production *In. Adaptation of Domestic Animals. Ed by E.S.E. Hafez, Lea and Febiger Philadelphia pp 74-93.*

Hall, H.T.B.(1977).Trypanosomiasis. *In Diseases and Parasites of livestock in the Tropics ITAS Longman.P.168.*

Hawking, F., Ramsden D.B. and Whytocks, S. (1973). The trypanocidal action of human serum and of Baboon plasma. *Transactions of the Royal Society for Tropical Medicine and Hygiene. 67: 501-516.*

Hornby, H.E. (1921) Trypanosomes and trypanosomiasis of cattle. *Journal of Comparative Pathology 34:211-240.*

Huan, C.N., Webb, L., Lambert, P.H. and Mischer, P.A. (1975). Pathogenesis of the anaemia in African trypanosomiasis:- Characterization and purification of a haemolytic factor, *Schweiz Medical Wschr. 105: 1582 - 1583.*

Hudson, K.M. Byner C., Freeman J. and Terry R.J. (1976). Immunodepression, high IgM levels and evasion of the immune response in murine trypanosomiasis. *Nature, 264: 256-258.*

Ige, K. and Amodu, A.A. (1975). *Report of the 14th Meeting of International ScientificCouncil for Trypanosomiasis Research and Control, Dakar Senegal p151 - 156.*

Ikede, B.O. (1979). Genital lesions in experimental chronic *Trypanosoma brucei.* infections in rams. *Research in Veterinary Science. 26: 145 - 151.*

Ikede, B.O.,Hill, D.H.and Akpokodje, J.U.(1973). *Nigerian Veterinary Journal 2:13-17.*

Ikede, B.O. and Losos, G.J. (1972). Pathology of the disease in sheep produced experimentally by *Trypanosoma brucei. Veterinary Pathology. 9: 278 - 289.*

Ikede, B.O. and Losos, G.J. (1975). Pathogenesis of *Trypanosoma brucei* infection in sheep 1. Clinical signs. *Comparative Pathology. 85: 23 - 31.*

Ikede, B.O. and Akpavie, S.O. (1982). Delay in resolution of trypanosome induced genital lesions in male rabbits infected with *Trypanosoma brucei.* and treated with diminazene aceturate. *Research in Veterinary Science. 32: 374 - 376.*

Ikede, B.O. (1981). "The understanding of the pathological effects of trypanosomiasis in ruminants as a basis for diagnosis. *Proceedings of the first national conference on Tsetse and Trypanosomiasis Research in Nigera. Ed. A.A. Ilemobade. August. 10 - 12. P. 96 - 107.*

Ikede, B.O. (1982). "Living and dying creatures great and small". *An inaugural lecture University of Ibadan, Nigeria.*

Ikede, B.O. (1986). African Trypanosomiasis "Proceedings *VIII[h] International Congress of Protozoology (1985) Ed. Odhiambo, T.O. Pergaman Press P. 368 - 378.*

Ikede, B.O., Elhassan, E. and Akpavie, S.O. (1988). Reproductive disorders in African trypanosomiasis. A review. *Acta Tropical 45,5-10.*

ILCA, Annual Report (1984). *The Livestock Productivity and Trypanotolerance group, Nigeria p. 45 - 46.*

ILRAD, 1979. Trypanotolerant livestock in West and Central Africa. *Monograph 122. ILCA, Addis-Ababa, Ethiopia. 148.*

ILRAD Annual report (1990). *Annual report of the International Laboratory for Research on Animal Diseases:- Trypanosomiasis:- p28 - 42.*

Ingh, T.S.G.A.M. Van den., Zwart, D., Miert A.S.J.P.A.M, Van., Schotman A.J.H (1976). Clinico-pathological and pathomorphological observations in *Trypanosoma vivax.* infection in cattle. *Veterinary Parasitology 2:237-250.*

Isoun, T.T. and Anosa, V.O. (1974a).The effects of experimental infection of *Trypanosoma vivax* on the reproductive organs of sheep and goats- A preliminary report. Nigerian Journal of Animal Production. 1: 143-150.

Isoun, T.T. and Anosa, V.O. (1974b). Lesions in the reproductive organs of sheep and goats infected with Trypanosoma vivax. *Z. Tropenmed. Parasitology. 25: 469 - 476.*

Isoun, T. T and Esuruoso, G.O.(1972). Pathology of natural infection of *Trypanosoma vivax* in cattle. *Nigerian Veterinary Journal 1:42-45.*

Jandl, J.H., Files, N., Barbet, S.B. and MacDonald, R.A. (1965). Proliferative response of the spleen and Liver to hemolysis. *Journal of experimental medicine. 122: 299 - 326.*

Jahnke, H.E. (1982). Livestock Production system in Livestock development in Tropical Africa. Kiel, FRG, Kieler. Wissenschaftsverdlag Vauk. Cited from Jahnke et al.,(1987). Livestock production in tropical Africa with special references to the tsetse-affected zones In. Livestock production in tsetse affected areas of Africa. *Proceedings of the Meeting of the African Trypanotolerant Network, held at Nairobi, Kenya. 23 - 27 Nov. 87.P.3*

Jahnke, H.E. Tacher, G., Kiel, P., and Rojat, D. (1987). Livestock production in Tropical Africa with special references to the tsetse-affected zones In. Livestock production in tsetse affected areas of Africa. *Proceedings of the Meeting of the African Trypanotolerant Network, held at Nairobi, Kenya. 23 - 27 Nov. 87. p.3*

Jeffcoate, I.A. and P.H. Holmes (1997). The effects of Trypanosomiasis on Reproduction in Domestic Ruminants. *In Trypanosomiasis and Leishmaniasis eds H. Htdo, J.S. Mottram, G.H. Coombs and P.H. Holmes. CAB. INT. 1997,P 335-346.*

Jenkins, G.C., McCrorie, P., Forsberg, C.M. and Brown M.J.Z. (1980). "Studies on the anaemia in rabbits infected with *Trypanosoma brucei. Journal of Comparative Pathology. 90: 107 - 121.*

Jennings, F.W., Murray, P.K:, Murray, M. and Urquhart, G.M. (1974). Immunosuppression in trypanosomiasis, the incorporation of iododeoxyuridine into the Lymph nodes of trypanosome-infected mice. *Transactions of the Royal Society for Tropical Medicine and Hygiene. 68: 151.*

Jennings, F.W. Murray, P.K., Murray, M. and Urquhart, G.M. (1974). Anaemia in trypanosomiasis, studies in rats and mice infected with *Trypanosoma brucei. Research in Veterinary Science. 16: 70 - 76.*

RAHIM LIBRARY

Jennings, F.W. (1976). The anaemia of parasitic infections. *Academic press. New York San Francisco, London . pp41-67 [edited by Soulsby].*

Johnson, B. H; Welsh, T. H and Juniewicz, P.E (1982). Suppression of LH and testosterone secretion in bulls following ACTH treatment. *Biology of reproduction 26:305-310.*

Jones, T.C. and Hunt, R.D. (1983). *Veterinary Pathology 5th ed. Lea and Febiger Philadephia. 1503-1543.*

Jones, T.W., Cunningham, I., Taylor, A.M. and Gray A.R. (1981). The use of culture derived metacylic Trypanosomes in studies on the serological relationships of stocks of *Trypanosoma brucei, gambiense. Transactions of the Royal Society for Tropical Medicine and Hygiene. 75: 560.*

Kaaya, G.P. and Odour-Okelo, D. (1980). The effects of *Trypanosoma congolense* infection on the testis and epididymis of the goat. *Bulletin of Animal Health and Production in Africa. 28:1-5.*

Kanyari, P.W.N. Allonby, E.W., Wilson, A.J., Munya, W.K. (1983). Some economic effects of trypanosomiasis in goats. *Tropical Animal Health and Production. 15: 153 - 160.*

Kobayashi, A and Tizard, I.R.(1976). The response to *Trypanosoma congolense* infection in calves: Determination of immunoglobulins IgG1, IgG2, IgM and C3 levels and the complement fixing antibody titres during the course of infection. *Tropenmendizin und Parasitolgie 27: 411-417.*

Kobayashi, A., Tizard, I.R. and Woo, P.T.K. (1976). Studies on the anaemia in experimental African trypanosomiasis II.The pathogenesis of the anaemia in calves infected with *Trypanosoma congolense. American Journal for Tropical Medicine and Hygiene. 25: 401-406.*

Krammer, J. (1966). Incidence of trypanosomes in West African Dwarf Sheep and goats in Nsukka, Eastern Nigeria. *Bulletin Epizootiological Diseases in Africa. 14: 423 - 428.*

Kupper, W., Wolter, M., Tscharf, T.(1983). Observations on Kob antelopes (Kobus Kob) in Northern Ivory coast and their epizootiological role in Trypanosomiasis transmission. *Zeit. Fur Ang. 277 - 283.*

Lawani, F.A.G. (1989). Pathology of the genitalia and endocrine glands of female goats infected with *Trypanosoma vivax. MSc. Thesis. A.B.U. Zaria.*

Leach, T.M., Roberts, C.J. and Macleannan K.J.R. (1965). 'Animal Trypanosomiasis' *WHO Training Course in trypanosomiasis booklet.*

Leeflang, P. (1975). The epizootiology of trypanosomiasis in ranch cattle (Shika Agricultural Research Station, Northern Nigeria) at some distance from known Primary foci of savanah tsetse. In. Proceedings 14th Meeting *International Science Council for Trypanosomiasis Research Contt. Publication No. 109: 94 - 100.*

Llewelyn, C.A., Luckins, A.G., Munro, C.D., and Perrie, J.(1987). The effects of *Trypanosoma congolense.* infections on the Oestrous cycle of the goat. *British Veterinary Journal 143: 423 431.*

Llewelyn, C.A., Munro, CD, Luckins, A.G., Jordt. T., Murray.M., Lorenzini E. (1988). The effects of*Trypanosoma congolense.* infection on the oestrus cycle of the Boran cow. *British Veterinary Journal. 144:379-387.*

Le-Ray,D.(1975). Structures antiqeniques de Trypanosoma brucei(Protozoa, kinetoplastida) Analyse immunoelectrophoretique et. etude comparative. *Ann. Soc. belge Med. Trop. 55: 129.*

Liggins, G.C. Greves, G.A., Kendall, J.Z. and Knox, B.S. (1972). The physiological roles of progesterone, oestradiol-17B Prostaglandndin F2alpha in the control of Ovine parturition. *Journal of Reproduction and Fertility Supplentary volume. 16:85-103.*

Lor, K.F., Pholpark, S., Siriwan, P., Leesirikul, N., Srikitjakarn, L., Staa K.C. (1986). *Trypanosoma evansi.* infection in buffaloes in North - East Thailand. II. Abortions. Tropical Animal Health and Production. 18: 103 - 108.

Losos,G. J.(1978). Infections caused by African Trypanosomes. In. G.J. Losos and A. Choinard (Editors).*Pathogenicity of Trypanosomes. IDRC 1329 Ottawa, Canada PP. 183 - 318.*

Losos, G.J. (1986). `Trypanosomiasis' *In infectious tropical diseases of domestic animals. Longman Scietific and Technical, p.183-318.*

Losos, G.J. and Chouinard, A. (1979) *"Pathogenicity of Trypanosomes" Publication. No. 132e IDRC, Ottawa Canada. PP 1 - 126.*

Losos, G.J. and amd Ikede, B.O. (1972). "Review of the pathology of diseasesof domestic and laboratory animalscaused by *Trypanosoma conglense., T. vivax., T. brucei., T. rhodesiense and T. gambiense." Veterinary Pathology (suppl.): 1 - 71.*

Losos, G.J., Paris, J, Wilson A.J., Dar, F.K (1973) Pathology of the disease in cattle caused by *Trypanosoma congolense. Bulletin of Epizootic Diseases of Africa 21: 239-248.*

Lourie, E.M and O`Connor, R. J. (1936) Trypanolysis in vitroby mouse immune serum. *Annals of Tropical Medicine and Parasitology. 30: 365-370.*

Luckins, A.G. (1975). Serum immunoglobulin levels and electrophoretic pattern of serum proteins in trypanosomes infected-bushbuck (Tragelaphus, scriptus). *Annals of Tropical Medicine and Parasitology. 69: 337-340.*

Luckins, A.G. (1976). The immune response of Zebu cattle to infection with *Trypanosoma congolense* and *T. vivax. Annals Tropical Medicine and Parasitology. 70: 133-145.*

Luckins, A.G., Mehlitz, D. (1978) Evaluation of indirect flourescent antibody test, enzyme-linked imminoasorbent assay and quantification of immunoglobulins in the diagnosis of bovine trypanosomiasis. *Tropical Animal Health and Production. 10: 149-159.*

Luckins, A.G. Llewelyn, G., Munro, C.D. and Murray, M.(1986). "Effects of pathogenic trypanosomes on the mammalian reproductive system". *Proceedings Internationalsymposium on the use of the Nuclear Techniques in studies of Animal Production and Health in different enviroments. IAEA, Vienna, Austria March 17 - 21: IAEA/SU - 292/34: PP 351 - 363.*

Lumsden, W.H.R. and Herbert, W.J.(1967). Phagocytosis of trypanosomes by mouse peritoneal macrophages. *Transactions of the Royal Society for Tropical Medicine and Hygiene. 61: 142-146.*

Maclennan, K.J.R. (1970). The epizootiology of trypanosomiasis in Livestock in West Africa.*In. H. W. Mulligan (Editor). The African Trypanosomiasis. Allen and Urwin, London, PP 751 - 765.*

Mack, S.D., Sumberg, J.E. and Okoli, C. (1985) Small Ruminants Production under pressure.The example of goats in South East Nigeria. *In Sumberg, J.E. and Cassaday, K. (Eds) Sheep and goats in humid West Africa. Proc. Workshop on Small Ruminants Production Systems in the humid zone of West Africa, Ibadan, Nigeria. 23rd - 26th January, 1984. ILCA Addis-Ababa, Ethiopia May, 1985 P.47-52.*

Mackenzie, P.K.I. and Cruickshank, J.G. (1973). Phagocytosis of erythrocytes and Leucocytes in sheep infected with Trypanosoma congolense. *Research in veterinary science, 15: 256 - 262.*

Maikaje, D.B., Sannusi, A., Kyewalabye, E.K. and Saror, D.I. (1991). The course of experimental *Trypanosoma vivax* infection in uda sheep. *Veterinary Parasitology. 38: 267 - 274.*

Mamo, E. and Holmes, P.H. (1975)."The erythrokinetics of Zebu cattle chronically infected with *Trypanosoma congolense. Research in Veterinary. Science. 18: 105 -106.*

Mansfield, J.M. (1978)."Commentary: Immunobiology of African Trypanosomiasis." *Cellular Immunology 39: 204-210.*

Margaret, Pinder, Juliane, Bauer; Alrun, Van Melick andFrancis,Fumoux (1988). Immune responses of Trypanoresistant and Trypanosusceptible cattle after cyclic infection with *Trypanosoma congolense. Veterinary Immunology and Immunopathology 18: 245 - 259.*

Masake, R.A. (1980). The pathogenesis of infection with *Trypanosoma vivax* in goats and cattle. *Veterinary Record. 107: 551 - 557.*

Masake, R.A., Pearson, T.W., Wells, P. and Roelants G.E.(1981). The in-vitro response to mitogens of Leucocytes from cattle infected with *Trypanosoma congolense, Clinical Experimental Immunology. 43: 583 - 589.*

Mason. I.L.(1951). Classification of West African Livestock. *Technical Communication 7 CAB Edinburgh.*

Maxie, M.G. and Valli, V.E.O. (1978). Hemodilution in bovine trypanosomiasis" *In. Pathogenicity of Trypanosomes. Ed. Losos, G. and Chouinard A. IDRC - 132e, Ottawa Canada. 145 - 150.*

Morrison, W.I., Roelants, G.E., Mayor-Withey, K.S. and Murray, M. (1978). Susceptibility of inbred strains of mice to *Trypanosoma congolense*. Correlation with changes, in spleen lymphocytes populations. *Clinical Experimental Immunology, 32:25-40.*

Morrison, W.I. and Murray M. (1979a). *Trypanosoma congolense*: inheritance of susceptibility to infection in inbred strains of mice. *Experimental Parasitology 48: 364-374.*

Morrison W.I. and Murray, M. (1979b) Lymhoid changes inAfrican trypanosomiasis. *In Losos G. and Chouinard A. eds)Pathogenicity of Trypanosomes, p154. IDRC, Ottawa, Canada.*

Morrison, I., Murray, M., McIntyre, I. (1981). Bovine trypanosomiasis. *FAO/SIDA, Follow-up seminar on veterinary Pathology. Faculty of Veterinary Medicine. University of Nairobi, Nairobi Kenya.*

Mortelmans, J and Kageruka I, (1976). Trypanotolerant cattle breeds in Zaire. *World Animal Review. 19:14-17.*

Moulton, J.E. and Sollod, A.E. (1976). "Clinical, serologic and pathologic changes in calves with experimentally induced *Trypanosoma brucei* infection." *American Journal of Veterinary Research. 37(1): 791 - 801.*

Murray, M. (1974). "The pathology of African trypanosomiasis" *Progress in immunology II. Amsterdam, N. Holland, Publishing Company, 181 - 192.*

Murray, M.(1978).Anaemia of bovine African trypanosomiasis:'An overview' In. *Proceedings workshop held at Nairobi, Kenya,20-23 Nov.,1978. Ed. by G. Losos and A. Chouinard. IDRC Ottawa, Canada, pp.121-127.*

Murray, M. (1979). "Anaemia of bovine African trypanosomiasis. "An overview" *In. Pathogenicity of Trypanosomes, Ed. Losos, G. and Chouinard A. IDRC - 132e, Ottawa Canada, 71-81.*

Murray, M. (1987). Trypanotolerance, its criteria and genetic and environmental influences. *In. Proceedings African trypanotolerant Livestock Net work. Livestock Production in tsetse affected areas of Africa. p.133 - 151.*

Murray, P.K., Murray, M., Wallace, M., Morrison, W.I. and McIntyre, W.I.M.(1977a). Trypanosomiasis in Ndama and Zebu cattle. Influence of weight of infection on the severity of the disease. *Proceedings of the 15th Meeting of the OAU/STRC International Scientific Council for Trypanosomiasis Research and Control, Banjul The Gambia. pp 482-487.*

Murray, M., Nguyen Huan,, C. Lambert, P.H., Gerber, H (1977b). Anaemia of African trypanosomiasis: demonstration of a haemolytic factor. *In. Proceedings of the 15th Meeting of OAU/STRC International Scientific Council for trypanosomiasis Research and Control, Banjul. The Gambia p.460-469.*

Murray, M. and Morrison, W.I.(1978). Parasitaemia and host susceptibility to African trypanosomiasis. *In. Proceedings workshop held at Nairobi, Kenya, 20-23 Nov.,1978. Eds. G. Losos and A. Chouinard, IDRC Ottawa, Canada, p. 71-81.*

Murray, M. and Morrison, W.I.(1981). Trypanotolerance: Its basis and future role in animal production in Africa. Isotope and Radiation in Parasitology. *Ivth. International Atomic Energy Agency, Vienna. p. 41-51.*

Murray, M., Clifford, D.J., Gettinby, G., Snow, W.F. and McIntyre, WIM. (1981) "Susceptibility of African trypanosomiasis of Ndama and Zebu cattle in an area of *Glossina morsitans sub. morsitans* challenge". *Veterinary Record 109: 503 - 510.*

Murray, M., Morrison, W.I. and White law, D. D. (1982). Host susceptibility of African trypanosomes Trypanotolerance. *Advances in Parasitology, 21: 1-68.*

Musoke, A. J., Nantulya, V.M., Barbet, A. F., Kironde, F and McGuire, T.C (1981). Bovine immune response to African trypanosomes: Specific antibodies to variable surface glycoprotein of *Trypanosoma brucei. Parasite Immunology 3:97 abstract.*

Mutayoba, B.M., Gombe, S., Kaaya, G.P., waindi, E.N. (1988a). Effects of chronic experimental *Trypanosoma congolense* infection on the ovaries, pituitary, thyriod and adrenal glands in female goats. Research in Veterinary Science. 44: 140 - 146.

Mutayoba, B.M., Gombe, S., Waidi E.N. and Kaaya, G.P. (1988b) Depression of ovarian function and plasma progesterone and Estradiol- 17B. In female goats chronically infected with T. congolese. *Acta Endocrinlogica 117:477-484.*

Mutayoba, B.M. Gombe, S., Kaaya, G.P. and Waindi, E.N.(1988c). Trypanosome-induced ovarian dysfunction. *Acta Tropica. 45: 225-237.*

Mutayoba, B.M. and Gombe, S. (1989). Effects of African Trypanosomiasis on plasma cortisol and thyroxine concentrations in goats. *Research in Veterinary Science 47:315-318.*

Mutayoba, B.M. Meyer, H.H.D., Osaso, J and Gombe, S. (1989). Trypanosome induced increase in prostaglandin PF2-alpha and its relationship with corpus luteum function in the goat. *Theriogenology 32: 545-555.*

Mutayoba, B.M. Eckersall, P.D., Jeffcoate, I.A. Cestnik, V, and Holmes, P. H.(1994). Effects of *T. congolense* infection in rams, on the pulsatile secretion of LH. and testosterone and response to injection of Gn/RH. *Journal of Reproduction and Fertility 102:425-431.*

Mutayoba, B.M., Eckersall, D.D., Jeffcoate I.A., Cestnik, v. and Holmes, P.K. (1995a) Alterations in plasma luteinizing hormone and testosterone concentration and responses to injection of GN/Rh in sheep infected with *T. congolense*. *Animal Reproduction Science*. 40: 203-214.

Mutayoba, B.M., Eckersall, P.D. Cestnik, V. Jeffcoate, I.A., Gray, C.E. amd Holmes, P.H. (1995b). Effects of *T. congolense* on pituitary and Adrenocortical function in sheep: Changes in the adrenal gland and cortisol secretion. *Research in Veterinary Science 58: 174-179.*

Mwambu, P.M. (1983). "Clinical and Pathological findings in experimental *Trypanosoma congolense* and *T. vivax* infection in cattle." *17th IRSCT - RC. Meeting, Arusha, Tanzania, 1981 P. 217 - 244.*

Nagle, R.D., P.A. , Lindsey, H.B., Sadun, E.H. Johnson, A.J., Berkaw, K.E. and Hildebrant P.K (1974). Experimental infections with African Trypanosomiasis of complement activation. *American Journal of Tropical Medicine and Hygiene, 23:15-26.*

Naylor, D.C. (1971). The haematology and histopathology of *Trypanosoma congolense* infection in cattle, II. Haematology."*Tropical Animal Health and Production.3: 159 - 168.*

Naylor, A.M. Porter, D.W.F. and Lincoln, D.W. (1990). Central administration of CRF in sheep: Effects on secretion of gonadotrophins, prolactin and cortisol. *Journal of Endocrinology 124:117-125.*

Nguyen Huan, C., Webb, L., Lambert, P.H., Miescher, P.A (1975). Pathogenesis of the anaemia in African trypanosomiasis characterization and purification of a haemolytic factor. *Schweizerische Medizinische Wochenschrift 105: 1582-1583.*

Nuru, S. (1974). Infectious bovine abortions in Northern Nigeria. *PhD. Thesis ABU Zaria, Nigeria.*

Nuru, S. (1985) Trends in Small Ruminants Production. In procedding: *National Conference on Small Ruminant Production in Nigeria, Oct., 6th - 10th, 1985: p.35-51 National Animal Production Research Institute. ABU Shika Zaria.*

Ogwu, D.(1983). Effects of *Trypanosoma vivax* infection on female reproduction in cattle. *PhD. Thesis ABU Zaria, Nigeria. P.103.*

Ogwu, D. and Njoku, C.O.(1987). Effects of pregnancy on the clinical manifestation of Bovine trypanosomiasis. *Veterinary Parasitology 24: 25 - 33.*

Ogwu, D. and Nuru, S. (1981). Transplacental transmission of trypanosomes in animals and man. *`A review' Veterinary Bullettin. 51: 381 - 383.*

Ogwu, D., Njoku, C.O., Osori, D.I.K., Ezeokoli, C.D. and Kumi-Diaka, J.(1984). Effects of experimental *Trypanosoma vivax* infection on fertility of heifers. *Theriogenology 22: 625-633.*

Ogwu, D., Njoku, C.O., and Osori, D.I.K. (1986). Effects of experimental *Trypanosoma vivax.* infection on first, second and third trimester pregnancy in heifers. *Theriogenology 25: 383 - 398.*

Ogwu, D. Njokwu, C.O. (1991) Genital lesions in experimental Trypanosoma congolense infection in heifers. *Animal Reproduction Science. 26: 1-11.*

Ogwu, D., Njokwu, C.O., and Ogbogu, V.C. (1992) Adrenal and thyroid disfunction in experimental *T. congolense* infection in cattle. *Veterinary Parasitology 42:15-26.*

O'Hara, H.B., Gombe, S. and King G.P. (1985). *VII[h] International Congress of Protozoology, Nairobi Kenya. June 22 - 25.*

Ojo, S.A., I.S. Kuteyi and I.F. Adu (1981). Studies on the oestrus phenomena in Yankasa and Uda breeds of sheep and the Yankasa crosses. *Nigerian Journal Animal Production 8:26(Abstract).*

Omeke, B.C.O. and Onuora, G.I. (1992). Comparative effects of *T. brucei* and *T. congolense* on reproductive capacity of boars in tsetse endemic zones. *Animal Reproduction Science 27:225-237.*

Orji, B.I., 1976. Studies on the biology of reproduction of the Nigerian Dwarf sheep. *PhD. Thesis University of Ibadan.*

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Orji, B.I., 1985. Research in Reproduction in Small Ruminants and their applicability in Nigerian Production Sytems. *In Proceedings:- National Conference on Small Ruminant Production in Nigerian. 6-10th Oct., 1985. P 70-84. National Animal Production Research Institute. ABU Shika Zaria.*

Orji, B.I., J., Steinbach, E.A. Olaloku and I.O.A., Adeleye (1976). Reproductive performance of the Nigerian dwarf sheep. *Nigerian Journal of Animal Production 3(2): 124-130.*

Orji, B.I., J. Steinbach, I.O.A., Adeleye (1977). West African Forest sheep or West African Dwarf Sheep. The case for a new name. *Paper presented at 4th Annual Conf. Nig. Soc. Anim. Prod. Ile-Ife, March, 1977.*

Orji,B.I., J. Steinbach, (1979). Oestrous cycle characteristics of the Nigerian Dwarf Sheep. 1.Duration of oestrous and length of oestrous cycle. *E.A. Agric. and forestry Journal.44:298-305.*

Orji, B.I., and J. Steinbach. (1980a). Gestation period and weight changes during pregnancy in the Nigerian Dwarf sheep. *Bullettin Animal Health and Production in Africa. 28:356-365.*

Orji, B.I., and J. Steinbach.(1980b). Postpartum anestrous period and lambing interval in Nigerian Dwarf Sheep. *Bullettin Animal Health and Production in Africa. 28: 368-371.*

Osburn, B.I. and Kennedy, P.C. (1981). Foetal infection. *In. current veterinary Therapy. Food animal practice. Howard, B.L. (ed.) W.S. Saunders, company, Philadelphia pp. 997 - 1000.*

Osinowo, O.A (1986) The economics of intensive sheep farming in Nigeria. *Paper presented at National Animal Production Research Institute. ABU Shika Zaria Seminar series November,5th 1986.*

Osinowo, O.A (1989). Reproduction in Yankasa sheep. A decade of Research at National Animal Production Reseach Institute, Ahmadu Bello University Zaria. *Unpublished report.*

Otchere, E.O. (1986). Traditional cattle production in the sub-humid zone of Nigeria. In: Von Kaufman R., Charter, S. and Blench R. (Eds). *Livestock System Research in Nigeria's sub-humid zone. Proceedings 2nd ILCA/NAPRI symposium held in Kaduna Nigeria. ILCA For Africa, Addis Ababa Ethiopia P. 110 - 140.*

Otchere E.O. (1981). The effects of supplementary feeding of tradtionally managed Bunaji cows In Von Kaufmann R., Chater S. and Blench, R. (Eds). *Livestock System Research in Nigeria's sub-humid zone p. 204 - 212 ILCA, Addis Ababa, Ethiopia.*

Otchere. E.O. and Kallah, M.S. (1990). Small Ruminants Production under traditional Management in Nigeria. In Osinowo, O.A., Abatan, A.A. (Eds*). The Nigerian sheep and goat production manual, NAPRI- ABU, Shika, Zaria - Nigeria.*

Otchere, E.O., Ahmed, H.U., Adenowo, T.K., Kallah, M.S., Bawa, E.K., Olorunju, S.A.S and Voh, A.A. (1987). Northern Nigeria: Sheep and goat production in the traditional Fulani agropastoral sector. *World Animal Review. 64: 50 - 55.*

Oyedipe, E.O., Voh, A.A., Marire, B.N. and Pathiraja N. (1986). Plasma Progesterone concentrations during oestrous and following fertile and non-fertile inseminations of Zebu heifers. *British Veterinary Journal. 142: 41 - 46.*

Pathiraja, N., Oyedipe, E.O., Voh, A.A. and P.M. Dawuda (1986). Accuracy of rectal palpation in the diagnosis of corpora lutea in Zebu cows. British Veterinary Journal. 142:467-471.

Patel, N.M., B.L., Avsatthi, K.S. Prajapti and D.D. Heranjai (1983). Effects of experimental *T. evansi.* infection on the reproductive organs of albino mice, rats, rabbits. A preliminary note. *Indian Journal of Animal Reproduction. 4:1:83-84.*

Pirofsky, B (1969). Auto-Immunization and auto immune haemolytic anemias. *1st edition Williams and Williams Co. Baltimorre USA p418-430.*

Pullan, N.B. (1979), "Productivity of White Fulani cattle on the Jos Plateau, Nigeria. I. Herd structure and reproductive performance. *Tropical Animal Health and Production. 11: 231 -238.*

Reuter, G., Pfeil, R., Stoll, S., Schauer, R., Kamerling, J.P., Verslius, C. and Vliegenthart, J. F. G.(1983). Identification of new sialic acids derived from glycoproteins of bovine submandibular gland. *European Journal of Biochemistry 134: 139-143.*

Reynolds, L. and Ekwuruke, J.O. (1988). Effects of *Trypanosoma vivax* infection on West African Dwarf Sheep at two planes of nutrition. *Small ruminants Research. 11: 175 - 188.*

Rickman, L.B. (1981). The effects of some African game animals sera in the BIIT in the *Trypanosoma (Trypanozoon) brucei species Trypanosomes*. Transactions of the Royal Society for Tropical Medicine and Hygiene. 75: 122.

RIM.(1992). Resource Iventory and Management, 1992. Livestock resources Volume 1. *Executive summary final report and Atlas. p.6-19.*

Ritz. H. (1916). Uber Rezidive bei Experimentelle Trypanosomiasis II. *Mitteilung Arch Schiffs Tropenhyg. 20: 397.*

Roberts, C.J. and Gray, A.R. (1973). Studies on trypanosome resistant cattle 1. The breeding and growth performance of Ndama, Muturu and Zebu cattle maintained under the same conditions of husbandry. *Tropical Animal Health and Production. 5: 211 - 233.*

Roeder, P.L., Scott J.M., Pegram, R.G. (1984). Acute Trypanosoma vivax infection of Ethiopian cattle in apparent abscence of tsetse. Tropical Animal Health Production. 16:141 - 147.

Saror, D.I. (1980). Observations on the course and Pathology of *Trypanosoma vivax* infection in Red Sokoto goats Research in Veterinary Science. 20: 36 - 38.

Schauer, R., Buscher, H.P and Gasals-Stenzel, J. (1974) Siallic acids: their analysis and enzymic modification in relation to the synthesis of submandibular gland glycoprotein. Biochemical Society Symposium 40:87-116.

Schauer R., Shukla, A.K., Chroder, C. and Muller, E.(1984). Anti-recognition function of sialic acids: studies with erythrocytes and macrophages. *Pure and Applied Chemistry. 56. 907-921.*

Scot, J.M. (1973). An interim report on the bovine and Camel situation in the Nagele (Borana) region. *Sidam Ministry of Agriculture Veterinary Department Report. Addis Ababa Ethiopia p. 7.*

Seed, J.R. (1972). *Trypanosoma gambiense* and *T. equiperdum*. Characterisation of variant specific antigens. *Experimental Parasitology. 31:98-108.*

Seed, J.R. (1977). The role of Immunoglobulins in immunity to *Trypanosoma brucei gambiense. International Journal of Parasitology. 7: 55-60.*

Sekoni, V.O; Kumi - Diaka, J. Saror, D., Njoku, C. (1988). The effects of *Trypanosoma vivax* and *Trypanosoma congolense* infection on the reaction time and semen characteristic in the Zebu bull. *British Veterinary Journal. 144: 388 -394.*

Sekoni, V.O. (1990). Effects of Novidium (Homidium Chloride) chemotherapy on genital lesions induced by *Trypanosoma vivax* and *Trypanosoma conglense* infections in the Zebu bull. *British Veterinary Journal. 146: 181 - 185.*

Sekoni, V.O. Saror, D.I. Njoku, C.O. Kumi - Diaka J.(1991) Effects ofNovidum(R) (Homidium chloride) chemotherapy on elevated spermatozoa Morhological abnormalities in the semen of Zebu bulls infected with *Trypanosoma vivax* and *Trypanosoma congolense. Animal Reproduction Science. p249 -258.*

Sekoni, V.O. (1994).Reproductive disorders caused by Animal trypanosomiasis. A. Review.*Theriogenology 42: 557 - 570.*

Shugaba, A., I. Umar., J. Omage., N.G. Ibrahim., J. Andrews., A.I. Ukoha., D.I. Sarror and K.A.N. Esievo (1994) Biochemical Differences (O-Acetyl and Glycolyl groups) in erythrocyte surface sialic acids of trypanotolerant N'dama and trypanosusceptible Zebu cattle. *Journal of Comparative pathology. 140: 91-95.*

Soudan, B., Tetaert, D, Degand, P and Baersma, A.(1992). Decrease in testosterone levels during an experimental African trypanosomiasis involvemnent of testicular LH receptor desensitization. *Acta Endocrinologica. 127:86-92.*

Steel, R.G.D and Torrie, J.H (1980) Principles and proceedures of statistics. *McGraw-Hill Book Co.,Inc.,NY Toronto, London.*

Stephen, L.E. (1966). Observations on the resistance of West African N'Dama and Zebu cattle to trypanosomiasis following challenge by wild *G. morsistans* from an early age. *Annals of Tropical Medicine and Parasitology. 60: 230 - 246.*

Stephen, L.E. (1970). Clinical manifestation of the trypanosomiasis in livestock and other domestic animals. In. H.W. Mulligan (Editor). *The African Trypanosomiasis, Goerge, Allen and Unwin, London p.774 - 794.*

Stewart, J.L. (1951). The West African short-horn cattle. Their value to Africa as trypanosomiasis-resistant animals. *Veterinary Record. 63: 454 - 457.*

Sumberg, J.E. (1985). Small ruminants feed production in a farming system content. *In: Sumberg J.E. and (Cassady K. (eds). Sheep and goats in humid West Africa. Proc. Workshop on Small Ruminants Production Systems in humid zone of West Africa, Ibadan-Nigeria, May 1985 P41-46.*

Takayanagi, T. and Enriquez, G.L. (1973). Effects of IgG and IgM immunoglobulins in *Trypamosoma gambiense*. infection in mice. *Journal of Parasitology. 59: 644-650.*

Takayanagi, T., Nakutaka, Y. and Enriquez, G.L. (1974). Attachment and ingestion of *Trypanosoma gambiense* to the rate macrophages by specific antiserum. *Journal of Parasitology. 60: 336-341.*

Tautor, G. and Idris, O.F (1973). Iron metabolism in Trypanosoma congolense infection in Zebu cattle: Serum iron and serum iron-binding capacity. *Research in veterinary science. 15: 24-32.*

Thurston, J.P. (1958). The effects of immune-sera in the respiration of *T. brucie* in-vitro. *Parasitology. 48: 463-467.*

Tilton, J.E. R.H. Hoffman, I.E. Berg, M.R. Light and M. L. Buchamen(1972). Influence of adrenalectomy on embryonic mortality in thermally stressed ewes. Journal of Animal Society. 34:605-608

Tizard, I.A., Nielson, K., seed, J.P. and Hall, J.E. (1978a). Biologically active products from African trypanosomes. *Microbiological Reviews. 42: 661 - 681.*

Tizard, I.R.; Holmes, W.L. and Nielson, K.(1978b) `Mechanism of anaemia in trypanosomiasis: Studies of the role of haemolytic fatty acids derived from *Trypanosome congolense. Tropenmedizin Und. Parasitologie. 29: 108-114.*

Tizard, I.R.; Nielson, K; Millons A. and Assouku.(1978c) Biologically active lipids generated by autolysis of Trypanosoma congolense. *In Pathogenicity of Trypanosomes. Eds. Losos, G and Choinard A. IDRC-132e Ottawa Canada.*

Touchberry, R.W. (1967). A study of Ndama cattle at the Mussia Animal husbandry station in Sierra Leone University. *III. Agricultural Experimental Station. Bull No. 724, Urbana III. 40 PP.*

Toure, S.M. Sere, M., Mbengue, M. and Dieye T. (1981). Trypanotolerance studies of comparative pathology on Dwarf Djallonke sheep and Sahelian Fulani sheep. *In. ISCTRC 15th Meeting at Arusha, Tanzania. OAU/Scientific Technical and Research Commission Publ. Wollo: 326 PP*

Urquhart, G.M. (1980). The pathogenesis and immunology of African trypanosomiasis in domestic animals. *Transasctions of the Royal Society for Tropical Medicine and Hygiene. 74: 726- 729.*

Valli, V.E.O., Forsberg, C.M. and Mcsherry, B.J. (1978). The pathogenesis of Trypanosoma congolense infection in calves. III. The neutropenia and myeloid response. *Veterinary Pathology. 16:96-107.*

Valli, V.E.O., Forsberg, C.M. and Mills J.N. (1979). Pathology of Trypanosoma congolense in calves. In.Losos, G. and chouinard, A (eds). *Pathogenicity of Trypanosomes, P. 179 IDRC Ottawa - Canada.*

Van den ingh, T.S. and D.J. Van Djik (1975). Pathology of chronic Trypanosoma brucei infection in rabbit. *Zentralblatt Fur Veterinamedizin, 22: 729-739.*

Van den Ingh, T.S., Zwart, D. Van Miert, A.S. and Schotman, A.J. (1976). Clinico-pathological and pathomorphological observations in Trypanosoma vivax. infection in cattle. *Veterinary Parasitology. 2: 237 - 250.*

Van Meirvenne, N., Janssens, P.G. and Magnus, E. (1975). Antigenic variation in syringe passaged populations of Trypanosoma (Trypanozoon) brucei. I. Rationalization of the experimental approach. *Annals Belgian society for Tropical medicine. 55: 1-15.*

Van - Meirvene, N., Magnus E. and Vervoort T. (1977). Comparison of variable antigen types produced by trypanosome strains of the subgenus Trypanozoom. *Annals Belgian society for Tropical medicine, 57: 409-423.*

Veh, R.W., Sander. M., Haverkamp, J. and Schaver, R. (1979) Demonstration of O-acetyl groups in ganglioside-bond sialic acids and their effects on the action of bacterial and mammlian neuraminidases. *Glycoconjugate Research, I: 557-559.*

Vickerman, K. and Barry, J.D. (1982). African Trypanosomiasis. *In. Cohen, S. and Warren K. (eds) Immunology of parasitic infections 2nd ed. Oxford Press 1982 PP 204 - 260.*

Voh. A.A., and Otchere E.O. (1989). Reproductive Performance of Zebu cattle under traditional agropastoral management in Northern Nigeria. Animal Reproduction Science,19: 191 - 203.

Vohradsky, F. (1971) Clinical signs, daily rate of infection, physical changes of the blood and pathomorphological changes in cattle artificially infected with trypanosoma vivax. *Revue D'elevage et de Medecine Ve'te'rinaire des Pays Tropicaux. 24:251-263.*

Waindi En, Gombe S, Odour-Okelo D. (1986). Plasma testosterone in *Trypanosoma congolense* infected Toggernburg goats. *Archives of Andrology 17:187-189.*

Wellhausen, S.R.and Mansfield. J.M. (1980) Lymphocytic function in experimental African trypanosomiasis III loss of lymphnode cell responsiveness. *Journal. Immunology 124:1183.*

Wintrobe, (1975). Diffuse intracellular coagulation. In: *Clinical haematology, Ed. Wintrobe, M.M. Lee Boggs, D.R. Bitheu I.T. Athens J.W. and Athens J.W. and Forester J. Lea and Febiger Philadelphia, 121-124.*

Woo, P. T. K(1969). The haematocrit centrifuge technique for the detection of trypanosomes in blood. *Canadian Journal of Zoology.47: 921-923.*

APPENDIX. 1.0.

STATISTICAL ANALYSIS OF THE CLINICAL DATA OF PREGNANT YANKASA AND WAD EWES INFECTED WITH *Trypanosoma vivax*. IN THEIR FIRST, SECOND AND THIRD TRIMESTERS OF PREGNANCY.

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App.1.1 Least square mean values of clinical observations of Yankasa and WAD ewes in first Trimester of pregnancy following *T vivax* infection.

Treatment groups	CLINICAL OBSERVATIONS Parasit.	Temp°C	% PCV	%Body wt.
Control Yankasa	0.0a	38.8a	28.22a	0.86a
Control .WAD	0.0a	38.92a	27.92a	3.71b
Infected.Yankasa	1.3b	37.1b	22.54b	-2.0c
Infected. WAD	1.01b	39.4a	23.58b	3.94d
SEM	0.27	0.9	0.71	1.1

Figures in the same column with different letters in superscript are significantly different($P<0.05$).

App.1.2. Least square mean values of clinical observations of Yankasa and WAD ewes in Second Trimester of pregnancy.

Treatment groups	CLINICAL OBSERVATIONS			
	Parasit.	Temp°C	%PCV	%Body wt.
Control Yankasa	0.0a	38.7a	30.22a	2.44a
Control WAD	0.0a	38.9a	31.87a	0.38a
Infected Yankasa	1.80b	39.6a	17.26b	-3.15b
Infected WAD	1.60b	39.8a	23.52c	-0.01b
SEM	0.29	0.8	1.38	1.8

Figures in the same column with different letters in superscript are significantly different($P<0.05$).

App.1.3. Least square mean values of clinical observations of Yankasa and WAD ewes in Third Trimester of pregnancy.

Treatment groups	CLINICAL OBSERVATIONS Parasit.	Temp°C	%PCV	%Body wt.
Control Yankasa	0.0a	38.97a	29.55a	1.18a
Control WAD	0.0a	38.90a	31.82a	3.68a
Infected Yankasa	1.42a	38.90a	16.45b	-5.63b
Infected WAD	1.60a	38.50a	19.05b	2.19c
SEM	0.24	0.9	1.7	2.16

Figures in the same column with different letters in superscript are significantly different($P<0.05$).

App.1.1.10: ANOVA of changes in Parasitaemia in Yankasa and WAD ewes in First Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	0.229	0.229	1.17	0.667
Treatments	2	24.174	12.087	0.24	0.0002*
Breed	1	0.386	0.386	0.30	0.588
Error	101	132.121	1.308	-	-
Corrected Error	107	157.341	-	-	-

*P<0.05

App.1 2.10: ANOVA of changes in Parasitaemia in Yankasa and WAD ewes in Second Trimester of Pregnancy.

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	0.108	0.108	0.07	0.788
Treatments	2	63.988	31.994	21.64	0.0001*
Breed	1	0.00	0.000	0.00	0.988
Error	100	147.824	1.478	-	-
Corrected Error	106	213.229	-	-	-

*P<0.05

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App.1.3.10: ANOVA of changes in Parasitaemia in Yankasa and WAD ewes in Third Trimester of Pregnancy.

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	2.116	2.116	2.06	0.154
Treatments	2	39.525	19.762	19.27	.0001*
Breed	1	0.188	0.188	0.18	0.670
Error	93	95.363	1.025	-	-
Corrected Error	99	140.194	-	-	-

*P<0.05

App.1.1.20: Analysis of Variance of Rectal Temp°c Scores of Yankasa and WAD ewes in First Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	4.192	4.129	0.28	0.595
Treatments	2	13.295	6.648	0.45	0.639
Breed	1	12.519	12.519	0.85	0.340
Error	101	1491.920	14.771	-	-
Corrected Error	107	1557.545	-	-	-

App.1.2.20: ANOVA of Rectal Temp°c Scores of Yankasa and WAD Ewes in Second Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	1757.664	1757.664	10.02	0.002*
Treatments	2	1729.444	864.722	4.93	0.009*
Breed	1	372.866	372.866	2.13	0.148
Error	100	17535.629	175.356	-	-
Corrected Error	106	21682.287	-	-	-

*P<0.05

App.1.3.20:ANOVA of changes in Rectal Temp°c in Yankasa and WAD ewes in Third Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	150.173	150.173	0.85	0.358
Treatments	2	699.628	349.814	1.98	0.143
Breed	1	1174.976	1174.976	6.67	0.0114*
Error	93	16393.226	176.271	-	-
Corrected Error	99	19215.448	-	-	-

*P<0.05

App.1.1.30: ANOVA of changes in PCV Values in Yankasa and WAD ewes in First Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	34.320	34.320	3.89	0.05*
Treatments	2	420.253	210.124	23.84	0.0001*
Breed	1	10.217	10.217	1.16	0.284
Error	101	890.279	6.815	-	-
Corrected Error	107	1371.602	- -	-	

*P<0.05

App.1.2.30: ANOVA for changes in PCV Values in Yankasa and WAD ewes in Second Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	145.741	145.741	4.38	0.0389*
Treatments	2	2013.590	1006.795	30.26	0.0001*
Breed	1	226.779	226.779	6.82	0.0104*
Error	100	3327.564	33.276	-	-
Corrected Error	106	6010.115	-	-	-

*P<0.05

App.1.3.30: ANOVA of PCV changes in Yankasa and WAD ewes in Third Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	234.903	234.903	5.20	0.0025*
Treatments	2	2699.494	1349.747	29.91	0.0001*
Breed	1	126.417	126.417	2.80	0.098
Error	93	4197.420	45.134	-	-
Corrected Error	99	7406.700	-	-	-

*P<0.05

App.1.1.40: ANOVA of percent changes in body weights of Yankasa and WAD ewes in First Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	53.838	53.838	2.52	0.1116
Treatments	2	231.605	115.803	5.41	0.0059*
Breed	1	189.437	189.437	8.85	0.0037*
Error	101	2161.556	21.401	-	-
Corrected Error	107	2859.517	-	-	-

*P<0.05

App.1.2.40: ANOVA of percent changes in body weights of Yankasa and WAD ewes in Second Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Wt	1	72.783	72.783	1.27	0.263
Treatments	2	247.994	123.997	2.16	0.121
Breed	1	9.490	9.490	0.170	0.685
Error	100				
Corrected Error	106				

App.1.3.40: ANOVA of percent changes in body weights of Yankasa and WAD ewes in Third Trimester of Pregnancy

Source	DF	Sum of Squares	Mean of Squares	F Value	P Value
Body Weight	1	140.476	140.476	1.78	0.185
Treatments	2	343.005	171.502	2.17	0.119
Breed	1	1403.887	1403.887	19.80	0.0001*
Error	93	7334.623	78.867	-	-
Corrected Error	99	9554.200	-	-	-

*P<0.05

APPENDIX 2.0

TABLES OF EFFECTS OF Trypanosoma vivax INFECTION ON WEIGHTS AND PERCENTAGE WEIGHTS OF FOETUSES OF YANKASA AND WAD EWES INFECTED IN THEIR FIRST, SECOND AND THIRD TRIMESTERS OF PREGNANCY AND THE EFFECTES OF NOVIDIUM CHEMOTHERAPY.

App. 2.1: WEIGHTS AND PERCENTAGE FOETAL WEIGHTS OF YANKASA EWES

Pregnancy Stages	First Untrtd.	First Treated	Second Untrt.	Second Treated	Third Untrt.	Third Treated	Controls
21days Pi	0.436g	1.49g	71.20g	126.84g	950.0g[10#]	-	-
7days PT	0.002%	0.007%	0.36%	0.70%	4.8%	-	-
					820.0g[12*]	-	-
					3.9%	-	-
					830.0g[12*]	-	-
					3.8%	-	-
28days Pi	1.110g	1.114g	-	-	-	-	
14days PT	0.0035%	0.0036%	-	-	-	-	-
49days Pi	-	-	134.7g	530.0g	910.0[32*]	930.0[23]g*	2,000g
35days PT	-	-	0.61%	2.24%	4.8%	4.2%	8.7%
						140.0[40]g+	2,300g
						5.8%	9.1%
							1,900g
							8.6%
Means(g)	0.0073	1.30	102.95	328.42	877.5	1035.0	2,067.0
(%)	0.004	0.0053	0.49	1.55	4.3	5.25	8.8

Percentage foetal weight is weight of foetus expressed as percentage of dam's weight
Pi = Post infection; PT = Post treatment
*Aborted foetuses; + case of dystocia;
Ewe died without aborting.
Figures in superscript are days Pi when ewe died or aborted or had dystocia

App.2.2 WEIGHTS AND PERCENTAGE FOETAL WEIGHTS OF WAD EWES.

Pregnancy Stages Controls	First Untrtd.	First Treated	Second Untrt.	Second Treated	Third Untrt.	Third Treated	
21 days Pi	none	none	Emd	28.37g	640.0[12]g*	-	-
7days PT	-	-	-	0.16%	4.47%	-	-
					590.0[13]g*	-	-
					4.2%	-	-
					725.0[14]g*	-	-
					5.2%	-	-
28 Days Pi	1.52g	1.64g	-	-	-	-	
14days PT	0.0072%	0.0070%	-	-	-	-	
49days Pi.	-	-	30.0g	180.0g	-	1,400.0g$	1,700g
35days PT	-	-	0.19%	0.86%	-	6.6%	7.6%
					-	1,350.0g$	1,900g
					-	7.2%	7.7%
					-	1,100.0g$	
1,800g							
					-	6.0%	7.6%
Means(g)	1.52	1.64	30.0	104.19	651.7	1,283.0	1,800
(%)	0.0072	0.0070	0.19	0.51	4.6	6.6	7.63

Percetage foetal weight is weight of foetus expressed as percentage of dams weight.
*Aborted fotuses.
$ Foetuses delivered alive.
Emd= early embryonic death.
Pi=Post infection. PT= Post treatment.