CLINICAL-PATHOLOGICAL AND ENDOCRINE CHANGES IN THE SERUM OF EWES ABORTING DUE TO *LISTERIA MONOCYTOGENES*

by

James L. Carter

B. S., Kansas State University, 1971
D. V. M., Kansas State University, 1973

A THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Graduate Pathology Group

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1976

approved by:

James E. Cook
Major professor

THIS BOOK CONTAINS NUMEROUS PAGES WITH THE ORIGINAL PRINTING BEING SKEWED DIFFERENTLY FROM THE TOP OF THE PAGE TO THE BOTTOM.

THIS IS AS RECEIVED FROM THE CUSTOMER.

ILLEGIBLE DOCUMENT

THE FOLLOWING DOCUMENT(S) IS OF POOR LEGIBILITY IN THE ORIGINAL

THIS IS THE BEST COPY AVAILABLE

TABLE OF CONTENTS

LIST OF FIGURES AND TABLES

INTRODUCTION

The method by which abortifacient agents trigger abortion is not clearly understood. Studies have been undertaken to determine some of the hormonal and clinical-pathological factors involved in normal parturition, but the mechanism of normal parturition is not completely understood either.

Listeria monocytogenes can cause abortion in late term ewes. The primary lesion is a placentitis with placental necrosis. This study was undertaken to relate some hormonal and clinical-pathological changes of normal parturient ewes to ewes aborting due to *Listeria monocytogenes*.

I: REVIEW OF LITERATURE

History

The first probable isolation of Listeria monocytogenes occurred in 1910 when Gustav Hulpers of Sweden isolated a bacteria from the liver of a rabbit. He called this organism Bacillus hepatis. The cultures were not retained so it was impossible to compare them with later isolations [15]. In 1926 Murray, Webb, and Swann isolated an organism in rabbits and guinea pigs in England. This organism caused a generalized infection with a marked mononuclear leukocytosis. They called the organism Bacterium monocytogenes [26]. A year later Pirie isolated an organism in the Tiger River Disease of South Africa. This organism caused focal liver necrosis in gerbils. He named the organism Listerella hepatolytica, but upon finding that the organism was identical to Bacterium monocytogenes, the name was changed to Listerella monocytogenes [33]. In 1937 Gill isolated the same organism from sheep and named it Listerella ovis. [8]. The term Listerella had been used for a form of plant life so Pirie proposed the name Listeria monocytogenes which is now used for Listeria monocytogenes isolated from all species of animals today [23].

Bacteriology

Listeria monocytogenes is a small gram positive organism which grows easily on most media under aerobic or microaerophilic conditions. It produces acid but no gas from several carbohydrates and is non-proteolytic [23]. The colonies are very small and beta hemolytic. The organism is a cocco-bacillus which is non-acid fast and non-spore forming. When cooled Listeria monocytogenes are motile, but at higher temperatures, they become sluggish [10]. Although it grows easily it is commonly difficult to isolate Listeria monocytogenes from infected material.[11]

Epidemiology

Listeria monocytogenes has a world-wide distribution with the possible exception of the tropics [19]. Isolations have been made in nineteen countries in all of the continents and from at least 18 species. These specied include members from the groups of birds, rodents, ungulates, carnivores and primates [23]. Some of the individual species include sheep [7], cattle [18], chickens (cited in 23), swine [2], foxes [4], chinchillas (cited in 23), ferrets [25], raccoons [6], horses [12], and man [3,21]. Outbreaks most commonly occur in winter or early spring. The outbreaks are usually sporadic, but up to 10% morbidity is possible [19].

Transmission

The method of transmission is unknown, but it appears to be an opportunist, and it also appears to be contagious to man [23]. Although Listeria monocytogenes is resistent in the enviroment, the most probable cause of outbreaks is carrier animals [19]. It is not definitely known if carriers or sick animals can spread the disease to man, but non-clinical carriers seem likely in both man and animals [11]. There is a definite, but poorly understood, relationship between silage feeding and the incidence of Listeriosis in livestock [11,19].

Pathogenesis

The pathogenesis of Listeric infection is poorly understood, but is thought to be different for disease of the central nervous system than for the reproductive system [11]. The possibility for the organism to reach the brain via the trigeminal nerve has been shown [1]. Lesions in a goat were traced along the trigeminal nerve to the brain stem after inoculation of Listeria monocytogenes into the conjunctiva. Similar results were reported in rabbits after inoculation into the conjunctiva or lip and in mice after inoculation of oral or nasal mucosa. Lesions in the brain stem were similar to the natural lesions in the brain [1]. An important step in the pathogenesis of Listeria monocytogenes abortions is considered to be the presence of the organism in the amniotic fluid. From there it can proceed to the placenta by direct invasion and via the fetal blood after fetal exposure by aspiration or swallowing [20].

The three main types of disease entities seen with Listeria monocytogenes include uterine infections with abortions, septicemia with miliary visceral necrosis and encephalitis [19,38]. Central nervous system lesions can occur in man, cattle, sheep, goats and swine. Septicemias are seen in man, cattle, sheep, swine, dogs, cats, and rodents. There are reports of abortions due to Listeria monocytogenes in man cattle, sheep and goats [38].

In ruminants, signs seen in the central nervous system infections vary only in severity. The signs include mental confusions, depression, head pressing, paralysis of one or more meduallary centers and unilateral paralysis of the seventh cranial nerve [19]. Deviation of the head to one side and circling movements are also observed [19,38]. The course of the disease in sheep usually runs a few hours to two days and in cattle from four to fourteen days. [19].

Gross lesions are not usually observed in the brain. Typical microscopic cuffing occurs in the brain. [19]. The lesions are most commonly present in the brain stem, being more severe in the medulla and pons and less severe in the thalamus and upper spinal cord [9,39]. The histological appearance of the lesions are considered virtually pathognomonic for Listeriosis [9]. A unilateral or bilateral metastatic suppurative opthalmitis is sometimes seen in ruminants with encephaliditities. The exact pathogenesis of the lesions is unknown [19,35]. In ruminants, with the exception of the goat, the encephalitic form is rarely observed in association with the abortion form [19,21].

The septicemic form is seen most commonly in neonates, [19] and in ruminants probably occurs only in neonates [1]. The lesions seen are miliary necrotic foci in the liver and less frequently in other organs [19,21].

Variations of the disease entity in ruminants are slight. Cattle and sheep have similar types of lesions with differences being largely quantitative. Cattle tend to have more chronic infections with small central nervous system lesions. Central nervous system signs and abortions both occur more commonly together in goats, than in cattle and sheep [21].

Species Effected

Listeriosis in swine is considered rare except perhaps in the Soviet Union. The most common form is septicemia in neonates with focal hepatic necrosis or less frequently skin lesions similar to pox may also appear [11]. Horses can abort, have septicemia with focal hepatic necrosis or less often show central nervous system signs [32]. Listeriosis is considered rare in dogs and cats [11]. Young chickens may succumb to Listeriosis, but most commonly the lesion is a massive area of myocardial degeneration [11]. Ferrets can harbour the disease without showing clinical signs [25].

Over 1,000 cases have been reported in man. Infants and people over 40, or people with some disabling condition are the most susceptible [11]. The breakdown of the types of syndromes in man is; meningitis or encephalitis, 33%; granulomatosis, 21%; septicemia, 21%; mononucleosis, 18%; and conjunctivitis, 6% [28]. Listeriosis can interrupt pregnancy in the human [11]. During the mononucleosis syndrome peripheral monocytes may be increased by as much as 6,000 times with no changes in other leukocyte counts [27]. This syndrome mimics, but is not true infectious mononucleosis of man [11].

Gross and Microscropic Lesions

Listeriosis can cause abortion in late gestation in ewes. The ewes appear clinically normal [19,[illegible]]. Ewes in late gestation aborted 7-11 days post intr-amniotic inoculation [illegible]. Various descriptions have been made of the gross placental lesions. These descriptions include a light coloured segmental appearance [10], white focal necrosis of cotyledons [22], intercotyledonary ulcerations of the chorio-allantois [13], and edema, thickening and reddish-brown discoloration of the intercotyledonary areas [10,22]. Endometritis was observed in other areas than the placentomes [13,30]. The gross lesions of the placenta are similar in both experimental and natural cases [13].

Histological changes of the placenta include extensive edema, diffuse leukocyte infiltration, a vasculitis of the chorio-allantois and necrosis and desquamation of the chorionic epithelium [13,31]. Fibrinoid necrosis and thrombosis of septal vessels at the feto-maternal interdigitation are common. Some of the early changes seen in the zone where the maternal caruncle and fetal cotyledoneconnect include bacteria in hemotomas near hyalinized tips of villiaand necrosis of the adjacent chorionic epithelium with neutrophils and plasma cells. In advanced stages numerous bacteria and zones of leukocytes can be seen [13].

The fetus may die in utero and be autolyzed [38] or may die shortly after birth from Listeric septicemia [36]. Fetal livers sometimes show miliary or submiliary, greyish-white foci [17,36]. About 75% of aborted lambs have focal necrosis or granulomas [5]. The livers have round borders, are friable, and are yellowish-brown [16].

In a sequential study of Listeric abortion in ewes, it was shown that 24 hours post intra-amniotic infection there is clouding of the amniotic fluid, edema of the allanto-amnio-chorion and organisms in the amniotic and chorionic epithelium. Thirty six hours post-infection, the lamb dies and post mortem autolysis begins. A reddish-brown exudate is present between the chorion and uterus and the uterus is separated from the allanto-amnio-chorion in the intercotyledonary areas, with edema and congestion. From 48-72 hours post-infection fetal hepatic necrosis may occur. At this same time the interdigitating areas of the placentomes become necrotic and thrombosis of the septal vessels occurs. Listeric colonies replace the autolytic chorionic epithelium. Calcification in the villar mesenchyme may occur along with progressive suppuration [21].

Lesions in the ewe appear to be restricted to hemmorrhage in the subcutis [16], skin [34], lungs [16,20,37], epicardium [20], kidney and mesenteric lymph nodes [37].

Summary

Listeria monocytogenes is a small gram positive bacteria of world wide distribution occurring in many species of animals. The method of transmission is not known, but carrier animals and silage feeding are partially responsible. The organism is capable of causing central nervous system syndromes, septicemias, and abortions. Ewes aborting due to Listeria monocytogenes are clinically normal with the predominant lesions occurring in the placentomes and placenta. On gross examination, the placenta is thickened, darkened and necrotic. Histological changes include edema, leukocytes, vasculitis of the chorio-allantois and necrosis of the chorionic epithelium. The aborted feti commonly are autolyzed and may have miliary

REFERENCES

1. Asahi, O., Hosoda, T., and Akiyama, Y.: Studies on the mechanism of infection of the brain with Listeria monocytogenes. Amer J Vet Res, 18, (1957): 147-157.

2. Biester, H. E., and Schwarte, L. H.; J Inf Dis, 64, (1939): 135-144.

3. Burn, C. G.: Proc Soc Exp Biol Med, 31, (1934):1095.

4. Cromwell, H. W., et al.: Science, 89, (1939): 293.

5. Dennis, S. M.: Perinatal lamb mortalities in Western Austrailia. FRCVS Thesis, Royal College of Veterinary Surgeons, London (1966).

6. Gifford, R. and Jungherr, E.: Cornell Vet, 37, (1947):39.

7. Gill, D. A.:"Circling Disease" of sheep in New Zealand. New Zealand Vet J, 87, (1931): 60-74.

8. Gill, D. A.: Aust Vet J, 13, (1937): 46.

9. Gitter, M.: Listeriosis in animals in Great Britain. Proc 3rd Int Symposium on Listeriosis, Bilthoven, (1967): 201-210.

10. Gorrie, C. J. R.: Ovine Abortion in Victoria. Aust Vet J, 38, (1962): 138-142.

11. Gray, M. L. and Killenger, A. H.: Listeria monocytogenes and Listeric infections. Bact Rev, 30, (1966): 309-382.

12. Grini, O.: Norsk Vet Tidsskr, 3, (1943).

13. Hartley, W. J., and Kater, J. C.: Perinatal disease conditions of sheep in New Zealand. New Zealand Vet J, 12, (1964): 49-57.

14. Hughes, K. L.: Listeria as a cause of abortion and neonatal mortality in sheep. Aust Vet J, 51, (1975): 97-99.

15. Hulpers, G.: Lefvernekros hoskanin orsaad af en ej forut beskrifuen bacterie. Svensk Veterinartidskrift.,16, (1911): 265.

16. Jeleff, W., Djurov, A., and Tomoff, T.: Einige Untersuchungen uber experimentell herrorgerufene Listerioseaborte. Mh Vet Med, 19, (1964): 773-778.

17. Jeleff, W., and Djurov, A.: Morphologische veranderungen det Feten bei spontaner listeriose infektion der Schafe. In: "Probleme der Listeriose" Symposium, Leipzig, 1968, edited by S. Liebe, and R. Degen, Leipzig: George Thieme (1969): 233-239.

18. Jones, F. S., and Little, R. B.: Arch Path, 18, (1934): 580-581.

19. Jubb, K. V. F. and Kennedy, P. C.: Pathology of Domestic Animals. Academic Press, New York, San Francisco, London (1970): 405-410.

20. Ladds, P. W.: Sequential studies on ovine Listeria abortion. Phd. Thesis, Kansas State University (1970).

21. Ladds, P. W., Dennis, S. M., Njoku, C. O.: Pathology of Listeric infection in domestic animals. Vet Bulletin, 44, (1974): 67-74.

22. MacDonald, J. W.: An outbreak of abortion due to Listeria monocytogenes in an experimental flock of sheep. Aust Vet J, 43, (1967): 564-567.

23. Merchent, I. A., Packer, R. A.: Veterinary Bacteriology and Virology. Iowa State University Press, Ames (1967).

24. Molello, J. A., and Jensen, R.: Placental pathology IV: Placental lesions of sheep experimentally infected with Listeria monocytogenes. Am J Vet Res, 25, (1964): 441-449.

25. Morris, J. A. and Norman, M. C.: J Bact, 59, (1950): 313.

26. Murray, E. G. D. et al.: J Path Bact, 29, (1926): 407-439.

27. Murray, E. G. D.: The story of Listeria, Flavelle Medallists address, Trans Royal Soc Canada, 48, (1953).

28. Murray, E. G. D.: A characterization of Listeriosis in man and animals. Canada Med Assn J, 72, (1955): 99.

29. Njoku, C. O., Dennis, S. M. and Cooper, R. F.: Listeric abortion studies in sheep I: materno-fetal changes. Cornell Vet, 62, (1972): 608-627.

30. Njoku, C. O., Dennis, S. M.: Listeria abortion studies in sheep II: feto-placental changes. Cornell Vet, 63, (1973): 171-192.

31. Njoku, C. O., Dennis, S. M.: Listeric abortion in sheep IV: histopathological comparison of natural and experimental infection. Cornell Vet, 63, (1973): 211-219.

32. Paterson, J. S.: Listeriosis, In: "Infectious Diseasesof Animals, Disease due to bacteria, Volume 1." edited by A. W. Stableforth and I. A. Galloway, London, Butterworths (1959).

33. Pirie, J. H. H.: Publ S African Inst Med Res, 3, (1927): 163-186.

34. Rittenbach, P. and Martin, J.: Ein Beitrag zur experimentellen Listeriose bei Haus und Versuchtieren. VIII Mitteilung Untersuchungen am experimentell erzeugten Listerienabort des Schafes. Arch Exp Vet Med, 19, (1965): 681-730.

35. Saunders, L. Z.; The eye In: "Joest, Handbuch der Speziellen Pathologischen Anatomie der Haustiere Volume III Mittelung, Untersungen an experimentell erzeugten Listerienabort des Schafes. Arch Exp Vet Med, 1, (1968): 739.

36. Seelinger, H. P. R.: "Listeriosis", Kofner, New York (1961).

37. Singh, C. H.: Pathology and bacteriology of abortion and perinatal death of young rabbits, sheep and goats. Phd thesis, Michigan State University. (1956).

38. Smith, H. A., Jones, T. C., Hunt, R. O.: "Veterinary Pathology". Lea and Febiger, Philadelphia (1972): 610-612.

39. Wuilleret, A., Desrres, P., Monteiro, L., Bouzakoura, C., and Wildi, E.: Contribution a l'etude du diagnostic batteriologique et histologique do la listeriose a l'occasion d'un enzootic ovine. Schweizer Arch. Tierheilk, 111, (1969): 622-641.

II. SERUM LEVELS OF PROGESTERONE, ESTRADIOL, AND CORTISOL IN EWES AFTER ABORTION DUE TO *LISTERIA MONOCYTOGENES*.

Introduction

The hormonal changes occurring at parturition in the ewe have been the topic of numerous investigations. The exact triggering mechanism or series of events is still not completely understood. One theory of the events leading up to parturition in the ewe was proposed by Liggins, Grieves, Kendall and Knox [58]. The theory proposes that the fetal pituitary initiates a series of events by releasing adrenocorticotrophic hormone (ACTH) which acts on the fetal adrenal to cause the release of glucocorticoids and a C-19 hormone. These steroids then act on the placentome to cause an increase in prostaglandin F 2 alpha (PGF 2 alpha) and estrogens, and a decrease of progesterone.

Evidence supporting the role of the fetal pituitary triggering parturition comes from experiments that showed that gestation is prolonged after fetal hypophysectomy [59]. Arginine vasopressin (AVP) and ACTH have been found in fetal plasma prior to parturition indicating the anterior and posterior pituitary are functional in the fetus [3].

Parturition can be delayed by bilateral adrenalectomy and can be initiated by the administration of ACTH and/or glucocorticoids to the fetal lamb [60]. The fetal adrenal has been shown to be active prior to term [55] with peak plasma levels near parturition, [28] and prior to the drop in progesterone levels [100]. There is not a significant correlation between fetal and maternal glucocorticoid levels [3]. Other investigators found about 15% of the fetal cortisol transferred to the mother from the fetus and 2% to the fetus from the dam [32].

Levels of plasma cortisol have been measured in the ewe and in the fetus by several investigators. Fetal levels of cortisol prior to parturition have been recorded as .4-2.27 micrograms/100ml. [32], .5-1.0 micrograms/ 100 ml. [63], around 1 microgram/ 100 ml. [58], and less than 2 micrograms/ 100 ml. [12]. At parturition, these levels increase to 8 micrograms/100 ml. [58], 7-26 micrograms/ 100 ml. [10], 10-35 micrograms/ 100 ml. [28], and 12-17 micrograms/ 100 ml. [12] respectively. The cortisol turnover rate in the fetus increases from 10.9 to 88.7 micrograms/ 100 ml. at parturition [28]. The cortisol levels of the pregnant ewe prior to parturition are in the range of 1.4 to 3.5 micrograms/ 100 ml. [49,65,74], and 1.06 to 1.67 micrograms/ 100 ml. [32].

PGF 2 alpha is considered to be leuteolytic in the ewe [48]. It has been shown that infusion of PGF 2 alpha in the vein of one uterine horn can cause regression of the corpus luteum on the same side [100]. Increases in PGF 2 alpha have been measured in the maternal caruncles and uterine vein plasma in dexamethasone induced labour [61]. The increase in uterine vein blood levels during the last 24 hours pre-parturition ranged from 1-2 ng./ml. to 7-17 ng./ml. in one study [100] and from less than 2 to 2.4-3.7 ng./ml. in another study [58]. Increases in PGF 2 alpha concentrations in the maternal placenta are from 100 to more than 600 ng./ g. wet tissue and the increases in the myometrium are from 50 to 300 ng./g. [58]. The increase in PGF 2 alpha in utero-ovarian plasma prior to parturition occurred about the same time as the increase in estrogen and was preceded by the decrease in progesterone [100]. This is further documented by another study in which progesterone levels remained constant after infusion of PGF 2 alpha but estradiol-17-beta rose from 5 to 165 pg./ml. in 8 hours after infusion [58]. Oxytocic effects of PGF 2 alpha in several species were described in one study [100], but were not observed in another study [58]. The investigators in the second study reported that this lack oxytocic activity may have been due to a requirement for low progesterone and high estrogen levels [58]. The second study indicated that PGF 2 alpha did enhance the response of the uterus to oxytocin and that elevated levels of fetal corticosteroids stimulated production and release of PGF 2 alpha independent of labour [58]. The pre-parturition increase in estrogen may also stimulate PGF 2 alpha synthesis and release and could be the link between the increased fetal corticosteroid levels and the increased maternal PGF 2 alpha levels [58]. Estrogen and PGF 2 alpha seem to have a stimulatory effect on each other. This observation could help to explain the rapid increase of both hormones at parturition.

Several properties of estrogen relating to the onset of parturition have been described [19]. Estrogen causes maturation of the uterus; enhances contractions in non-pregnant animals; dilates blood vessels; increases cell permeability and aids electrical conductance of the myometrium. It also increases the response of the myometrium to oxytocin [19]. Some investigators believe that estrogen is the probable final trigger of parturition by increasing the uterine blood flow; possibly causing myometrial contractions and overcoming the "progesterone block". These investigators also noted an increase in the blood levels of oxytocin in non-pregnant sheep given estrogens following vaginal distention [14]. Conflicting views are proposed by other investigators who caused premature parturition by giving fetal lambs ACTH and noted in some cases parturition in the absence of a significant rise in estradiol-17-beta [58]. The concept that a direct stimulation of the myometrium occurrs is not favored by all investigators. During pregnancy estrogens are formed by the placenta. The fetus and the placenta both can metabolize estrogens [39]. The maternal peripheral blood levels of estrogen are relatively low prior to parturition. Reported blood levels of estrogen are 20-40 pg./ml., [20], and 40 pg./ml. [27] five days prior to parturition and 29.6 pg./ml. [20], and 20 pg./ml. [100] two days prior to parturition. There is a marked increase at parturition to 75-411 pg./ml. [20], 396-734 pg./ml. [27], 232 pg./ml. [14], 880 pg./ml. [100], and 31-59 pg./ml. [58]. Estrone and estradiol-17-beta have a ratio of 1.9 to 1 [100].

Two possible functions of progesterone include suppression of uterine activity and suppression of PGF 2 alpha. Progesterone is required for the maintenance of early pregnancy. Twenty mg. per day of progesterone can maintain pregnancy in ewes up to 60 days [69] and 1 mg. of progesterone with 25 mg. estrone can maintain pregnancy in very early pregnancy [43]. The main source of progesterone for the first 50 days is believed to be the ovary. During this period of time there is no significant difference in progesteronelevels between pregnant and non-pregnant ewes in the luteal stage of the estrous cycle [86]. Removal of the ovaries between 66-114 days has no effect on progesterone levels or pregnancy [92]. After 50 days placental progesterone secretion is the major source [64]. The increase in placental progesterone may be due to the rapid increase in uterine volume [9]. The progesterone levels in late pregnancy in the placenta of both intact and ovariectomized ewes reaches 4-9 micrograms/kg. of tissue [86]. Peripheral blood levels increase to 40 ng./ml. at 15 days prior to parturition [27]. One day prior to parturition the progesterone levels are 7.6 ng./ml. (single lambs), 13.5 ng./ml. (twins) [11], 8-12 ng./ml. [70], and 17 ng./ml. [58]. There is a rapid decrease at the time of parturition to .3 ng./ml. (single lambs), .3 ng./ml. (twins) [11], 2.1 ng./ml. [44] and 1.8 ng./ml. [58] respectively. In other instances the decrease follows parturition [86,92] or occurrs before parturition [27]. This drop is not always consistent [11]. The fall in progesterone levels around parturition is unlikely to be a major factor initiating birth in the ewe, but it does help to increase the efficiency of the uterus [58]. Parturition can occur without low progesterone levels as shown by the normal time of delivery in ewes given 80 mg. of progesterone over the last week pregnancy. However, there was a decrease in the amplitude of pressure waves of the uterus [15]. In cattle infected with <u>Vibrio fetus</u>, the peripheral levels of progesterone declined at the time of fetal death much like normal parturition. This may be due to placental dysfunction or products from the infected fetus [72].

Prolactin and oxytocin levels both increase in the peripheral plasma near delivery. Prolactin values stabilize at 90 days at 2.4-6.0 ng./ml. and gradually increase till a few days prior to birth. At delivery prolactin levels increase to 400 ng./ml. [3]. Oxytocin levels are also maximal at this time [40].

<u>Materials and methods</u>

Animals: Suffolk and crossbred ewes in the last third of gestation were housed in a controlled enviroment (24 ± 2 C). Twelve test ewes were inoculated intravenously in the jugular vein with 5 ml. of six-hour broth culture of <u>Listeria monocytogenes</u>. Four control ewes were inoculated with 5 ml. of broth only. Fifteen ml. blood samples were collected daily by venapuncture of a jugular vein. Serum was separated and kept at -20 C until assay.

Radioimmunoassay of hormones:

Progesterone: Two-tenths of one ml. of serum was extracted with 5 ml. of fresh ether. The ether fraction was dried and reconstituted with 1 ml.

of assay buffer and the assay buffer was halved for duplicate assay. The progesterone concentration was determined by the procedure of Garza et al.[45]. (antibody S-33 #5) Sensitivity of the assay was 10 pg. and the antiserum cross-reacted with only 6.5% of desoxycorticosterone and 4.5% of testosterone.

Estradiol: One ml. of serum was extracted with fresh ether. The ether fraction was dried and reconstituted with one ml. of assay buffer and the buffer was pipetted into two fractions for duplicate assay. The concentration of estradiol was determined by the procedure of Abraham et al.[2] (antibody S 1554 #6), which is specific for estradiol-radioimmunoassay.

Cortisol: One-tenth of one ml. of serum was precipitated with 0.4 ml. of absolute ethanol, then 10 microliters of the ethanol fraction was pipetted to 0.5 ml. of assay buffer for radioimmunoassay, according to Abraham et al.[1], (antibody S162 #3). Duplicate assays were performed for each serum sample. The antibody cross reacted slightly with the following steroids: Corticosterone, 9.0%; 17 alpha-hydroxyprogesterone 8%; cortisone 6.0%, and 11-desoxycortisol 6.0%.

Statistics: Polynomial regression coefficients were derived from standard samples with Wang's computer for the formula:

$$\log y = a_0 + a_1x + a_2x^2 + a_3x^3$$

where y = hormone concentration
x = % of labeled hormone bound

The regression coefficients were used to determine hormone concentrations in the unknown samples. Student's t-test was used for comparison and differences were considered significant when P values were less than 0.05.

Results

Listeria monocytogenes caused abortion in all 12 test ewes 9 days after inoculation (8.6 ± 0.4 days, range from 6–10 days).

The serum levels of progesterone obtained from both test and control ewes were similar (Figure 1). Progesterone ranged from 5–10 ng./ml. from 1 to 9 days before parturition and dropped at parturition to a low of 1 ng./ml. 1 day post-partum (test ewes) and 2 days post-partum (control ewes).

Estradiol in the control ewes increased significantly (from 175 to 450 pg./ml.) at parturition. Test ewes also had increased estradiol levels (from 130 to 200 pg./ml.), but the increase was not statistically significant. Estradiol of the control ewes dropped to the pre-partum levels within two days post-partum (Figure 2).

Cortisol in the peripheral blood increased after the test ewes were inoculated with Listeria monocytogenes. The cortisol levels were 69 ng./ml. one day post-inoculation; dropped to 50 ng./ml. three days post-inoculation, then continued to decrease and leveled off at 35 ng./ml. 9 days post-inoculation. No increase in cortisol was observed at abortion. The control ewes had gradually increased serum cortisol levels ranging from 27 ng./ml. nine days before parturition to 40 ng./ml. the day before parturition. On the day of delivery serum cortisol peaked at 70 ng./ml. (Figure 3).

Discussion

The results show that progesterone changes in aborting ewes infected with Listeria monocytogenes and in normally parturient ewes at delivery are similar. The trends observed in control ewes were similar to those reported by others [23,58,89,98,99]. A drop in progesterone has been reported within a few days after inoculating with Actinobacillus seminis [89]. Smith and Hughes [89] thought placental lesions caused the decrease as placental progesterone is considered the major source of progesterone in sheep during late pregnancy. Although *Listeria monocytogenes* also causes placental lesions,[57] in this study no decrease in progesterone occurred near parturition. Since progesterone normally decreases at or shortly after parturition, the decrease in *Listeria monocytogenes* infected ewes could result from (1) the expected decrease at parturition, (2) the destruction of placental progesterone production, or (3) both factors.

The significant increase in serum estrogen of controls at parturition was in essentially good agreement with the results reported by others[14,20,23,58]. The slight increase in estrogen of infected ewes at abortion was not statistically significant. As *Listeria monocytogenes* causes necrosis of the placentomes[57], the main source of estrogen near parturition may be the placenta and adrenal gland. Necrosis of the placenta and exhaustion of the adrenals[98] could lower estrogen production for the anticipated estrogen surge.

The initial increase of cortisol on the day after test ewes were inoculated can be explained as a response to the infection. The increase in serum cortisol in the controls at parturition agrees with two earlier reports[23,97] although it was not observed in two others[33,73]. Stress associated with parturition or the normal hormonal triggering mechanism of parturition may explain the increase. Research on human beings has shown a rise in cortisol at parturition, thought to be brought on by labour stress[54]. An increase in fetal cortisol has been reported in sheep[10,12,26,58], but only a small portion is transferred to the dam[10,32]. So, fetal cortisol is an unlikely source for the maternal increase at parturition. Our test ewes had no increase in cortisol at parturition, perhaps because the adrenals were exhausted by the infection.

Listeria monocytogenes appears to induce abortion in sheep without initiating all standard triggering mechanisms. Placentomes being destroyed seem to be the most probable reason.

Summary

Estradiol, progesterone and cortisol were measured by radioimmunoassay in peripheral serum of pregnant ewes infected with *Listeria monocytogenes* and in normal pregnant controls. Progesterone had decreased in both groups at parturition or abortion. Estradiol and cortisol of control ewes had a markedly increased level at parturition. The infected ewes had significantly increased levels of cortisol for 3 days after inoculation, but it returned to pre-inoculation levels for the remainder of gestation. Serum levels of cortisol did not change and estradiol levels increased only slightly at abortion by infected ewes.

REFERENCES

1. Abraham, G. E., Buster, J. E. and Teller, R. C.: Radioimmunoassay of plasma cortisol. Analyt Letters, 5, (1972): 757-765.

2. Abraham, G. E., Hopper, K., Tulchinsky, D., Swerdloff, R. S., and Odell, W. D.: Simultaneous measurement of plasma progesterone, 17-hydroxy-progesterone, and estradiol-17-beta by radioimmunoassay. Analyt Letters, 4, (1971): 325-335.

3. Alexander, D. P., Britton, H. G., Forsling, M. L., Nixon, D. A., and Ratcliffe, J. G.: The concentrations of adrenocroticotophin, vasopressin, and oxytocin in the fetal and maternal plasma of the sheep in the latter half of gestation. J Endocr, 49, (1971): 179-180.

4. Alexander, D. P., Britton, H. G., Nixon, D. A., Ratcliffe, J. G., and Redstone, D.: Corticotrophin and cortisol concentrations in the plasma of the chronically catheterised sheep fetus. Biol Neonate, 23, (1973): 184-192.

5. Archer, D. F.: Effects of prostaglandin F 2 alpha on cholesterol biosynthesis by human corpora lutea of pregnancy. Bio of Reprod, 9, (1973): 95.

6. Ash, R. W. and Heap, R. B.: Oestrogen, progesterone and corticosteroid concentrations in peripheral plasma of sows during pregnancy, parturition, lactation and after weaning. J Endocr, 64, (1975): 141-154.

7. Balfour, W. E., Comline, R. S., and Short, R. V.: Secretion of progesterone by the adrenal gland. Nature, 180, (1957): 1480-1481.

8. Baird, D. T., Collett, R. A., and Land, R. B.: The pattern of progesterone secretion by the autotransplanted ovary of the ewe in response to ovine luteinizing hormone and HCG. J Reprod Fert, 25, (1971): 308-309.

9. Barcroft, J.: Researches on prenatal life. Blackwell Scientific Publications, Oxford. (1946).

10. Bassett, J. M., and Thorburn, G. D.: Foetal plasma corticosteroids and the initiation of parturition in sheep. J Endocr, 44, (1969): 285-286.

11. Bassett, J. M., Oxborrow, Tana J., Smith, I. C. and Thorburn G. D.: The concentration of progesterone in the peripheral plasma of the pregnant ewe. J Endocr, 45, (1969): 449-457.

12. Bassett, J. M., and Thorburn, G. D.: Circulating levels of progesterone and corticosteroids in the pregnant ewe and its fetus. In: the endocrinology of pregnancy and parturition. Edited by C. G. Pierrepoint, Cardiff, Alpha Omega Alpha., (1971): 126-140.

13. Beck, A. B.: Studies on the excretion of oestrogens by pregnant ewes. Aust J Agric Res, 1, (1950): 322-337.

14. Bedford, Cecelia A., Challis, J. R. G., Harrison, F. A. and Heap R. B.: The role oestrogens and progesterone in the onset of parturition in various species. J Reprod Fert., Suppl. 16, (1972): 1-23.

15. Bengtsson, L., and Schofield, B. M.: Progesterone and the accomplishment of parturition in sheep. J Reprod Fert, 5, (1963): 423-431.

16. Bland, K. P., Horton, E. W., and Poyset, N. L.; Levels of prostaglandin F 2 alpha in the uterine venous blood of sheep during the oestrus cycle. Life Sci, 10, (1971): 509-517.

17. Bryant, G. D., Greenwood, F. C., Kann, G., Martinet, J., and Denamur, R.: Plasma prolactin in the oestrus cycle of the ewe: effect of pituitary stalk section. J Endocr, 51, (1970): 405-406.

18. Caldwell, B. V., Rowson, L. E. A., Moor, R. M. and Hay, M. F.: The utero-ovarian relationship and its possible role in infertility. J Reprod Fert, Suppl 8, (1969): 59.

19, Carsten, M. E.: Regulation of myometrial composition growth and activity. In: Biology of Gestation, Vol. 1 Edited by N. S. Assali, Academic Press, New York and London (1968).

20. Challis, J. R. G., Harrison, F. A., and Heap, R. B.: Sharp increase in free circulating oestrogens immediately before parturition in sheep. Nature, 229, (1971): 208,.

21. Challis , J. R. G., Harrison, F. A. and Heap, R. B.: Uterine production of oestrogen and progesterone at parturition in the sheep. J Reprod Fert, 25, (1971): 306-307.

22. Challis, J. R. G., Harrison, F. A., and Heap, R. B.: The estraction of oestrogens, and the rate of secretion of oestrone and oestradiol-17-beta by the uterus in the pregnant sheep. J Endocr, 61, (1974): 277-284.

23, Chamley, W. A., Buckmaster, Joan M., Cerini, Mildred E., Cumming, I. A., Boding, J. R., Obst, J. M., Williams, A., and Winfield, C.; Changes in the levels of progesterone, corticosteroids, estrone, estradiol-17-beta, luteininzing hormone, and prolactin in the peripheral plasma of the ewe during late pregnancy and at parturition. Biology of Reprod, 9, (1973): 30-35.

24. Chan, T., and Klopper, A.: The variability of plasma oestradiol concentration in late pregnancy. J of Obst and Gyn of the British Commonwealth, 81, (1974): 357-360.

25. Chard, T., Boyd, N. R. H., Forsling, M. L., McNeilly, A. S., and Landon, J.: The development of a radioimmunoassay for oxytocin: the extraction of oxytocin from plasma and its measurement during parturition in human and goat blood. J Endocr, 48, (1970): 223-234.

26. Comline, R. S., Nathanielsz, P. W., Paisey, R. B. and Silver,

Marian: Cortisol turnover in the sheep foetus immediately prior to parturition. J Physiol, 210, (1970): 141-142.

27. Comline, R. S., and Silver, M.: The release of adrenaline and noradrenaline from the adrenal glands of fetal sheep. J Physiol, 156, (1961): 424-444.

28. Comline, R. S. and Silver, M.: The composition of foetal and maternal blood during parturition in the ewe. J Physiol, 222, (1972): 233-256.

29. Concannon, P. W. and Hansel, Wm.: Changes in plasma progesterone and corticoids at parturition in the bitch. Biology of Reprod, 9, (1973): 104.

30. Cox, R. I., Mattner, P. E., Shutt, D. A., and Thorburn, G. D.: Ovarian secretion of oestradiol during the oestrus cycle in the ewe. J Reprod Fert, 24, (1971): 133-134.

31. Davis, S. L., Reichert, L. E. and Niswender, J. R.: Serum levels of prolactin in sheep as measured by radioimmunoassay. Biology of Reprod, 4, (1971): 145.

32. Dixon, R., Hyman, A., Gurpide, E., Dyrenfurth, I., Cohen, H., Bowe, E., Engel, T., Daniel, S., James, S., and Vande Wiele, R.: Feto-maternal transfer and production of cortisol in the sheep. Steroids, 16, (1970): 771-789.

33. Drost, M., Kumagai, L. F., and Guzman, Margaret: Sequential foetalmaternal plasma cortisol levels in sheep. J Endocr, 56, (1973): 483-492.

34. Dukes, M., Chester, Rosemary, and Atkinson, Patricia: Effects

of oestradiol and prostaglandin F 2 alpha on the timing of parturition in the rat. J Reprod Fert, 38, (1974): 325-334.

35. Edgar, D. G., and Ronaldson, J. W.: Blood levels of progesterone in the ewe. J Endocr, 16, (1958): 378-384.

36. Emmens, C. W.: Presiding over , Reproduction in the female. combined session of the Australian Society for Reproductive Biology and the Australian Endocrine Society, J Reprod Fert,24, (1971):133.

37. Fairclough, R. J., Hunter, J. T., and Welch, R. A. S.: Peripheral plasma progesterone and utero-ovarian prostaglandin F concentrations in the cow aroudd parturition. Prostaglandins,9, (1975): 901-914.

38. Findlay, J. K., and Cox, R. I.: Oestrogens in the plasma of the sheep foetus. J Endocr, 46, (1970): 281-282.

39. Findlay, J. K., and Seamark, R. F.: The biosynthesis of oestrogens in the ovine foeto-placental unit. J Reprod Fert, 24, (1971): 141.

40. Fitzpatrick, R. J. and Walmsley, C. R.: The release of oxytocin during parturition, In: "Advances in Oxytocin Research", Edited by J. H. M. Pinngton, Pergamon, London and New York (1965): 51-71.

41. Flint, A.P. F., Anderson, Anne B. M., Patten, P. T., and Turnbull, A. C.: Uterine venous prostaglandin F and oestrogen levels during ovine parturition: acute effects of cervical stimulation. J Endocr, 61, (1974): xxxv-xxxvi.

42. Flint, A. P. F., Anderson, Anne B. M., and Turnbull, A. C.: Control of utero-ovarian and peripheral venous plasma progesterone by beta-sympathomimetic drugs in pregnant sheep. J Endocr, 63, (1974): 253-254.

43. Foote, W. D., Gooch, L. F., Pope, A. L., and Casida, L. E.: The maintenance of early pregnancy in the ovariectomized ewe by injection

of ovarian hormones. J Anim Sci, 16, (1957): 986-989.

44. Fylling, P.: The effect of pregnancy, ovariectomy and parturition on plasma progesterone levels in sheep. Acta Endocr, 65, (1970): 273-283.

45. Garza, R., Burns, B., Manlimos, F. and Abraham, G. E.: Radio-immunoassay of plasma progesterone without chromatography. Analyt Letters, 8, (1975): 225-232.

46. Gleeson, A. R., and Thorburn, G. D.: Selected factors that affect the measurement of plasma progesterone concentrations in pregnant ewes. Aust J Biol Sci, 27, (1974): 659-669.

47. Goding, J. R., Catt, K. J., Brown, J. M., Kaltenback, C. L., Cumming, I. A., and Mole, B. J.: Radioimmunoassay for ovine lutenizing hormone: secretion of lutenizing hormone during estrus and following estrogen administration in the sheep. Endocrinology, 85, (1969): 133-142.

48. Goding, J. R., Cain, M. C., Cerine, M., Chamley, W. A., and Cumming, I. A.: Prostaglandin F 2 alpha the luteolytic hormone in the ewe. J Reprod Fert, 28, (1972): 146-147.

49. Harrison, F. A., and Heap, R. B.: Progesterone secretion by the autotransplanted adrenal and ovary in a pregnant sheep. J Physiol (London) 196, (1968): 43-45.

50. Hawk, H. W. and Bolt, D. J.: Luteolytic effect of estradiol-17-beta when administered after midcycle in the ewe. Bio Reprod, 2, (1970): 275-278.

51. Hindson, J. C., Schofield, B. M., Turner, C. B., and Wolff, H. S.: Parturition in the sheep. J Physiol (London), 181, (1965): 560-567.

52. Hixon, J. E., and Clegg, M. T.: Influence of the pituitary on oavrian progesterone output in the ewe. Effects of hypophysectomy and

gonadotropic hormones. Endocrinology, 84, (1969): 828-834.

53. Hoffman, B., Schams, D., Gimenez, T., Ender, M. L., Herrmann, Ch., and Karg, H.: Changes of progesterone, total oestrogens, corticosteroids, prolactin and LH in bovine peripheral plasma around parturition with special reference to the effect of exogenous corticoids and a prolactin inhibitor respectively. Acta Endocr, 73, (1973): 385-395.

54. Jolivet, A., Blanchier, H., and Gautray, J. P.: Blood cortisol variations during late pregnancy and labour. Am J Obstet Gynecol, 119, 6, (1974): 775-783.

55. Jones, I. C., Jarrett, I. C., Vinson, G. P. and Potter, K.: Adrenocorticosteroid production of foetal sheep near term. J Endocr, 29, (1964): 211-212.

56. Killian, D. B., Garverick, H. A., and Day, B. N.: Peripheral plasma progesterone and corticoid levels at parturition in the sow. J Ani Sci, 37, (1973): 1371-1375.

57. Ladds, P. W., Dennis, S. M., and Njoku, C. O.: Pathology of Listeric infection in domestic animals. Vet Bulletin, 44, (1974): 67-74.

58. Liggins, G. C., Grieves, Susan A., Kendall, June A., and Know, B. S.: The physiological roles of progesterone, oestradiol-17-beta and prostaglandin F 2 alpha in the control of ovine parturition. J Reprod Fert., Suppl 16, (1972): 85-103.

59. Liggins, G. C.: J Endocr, 45, (1969): 515-523.

60. Liggins, G. C., and Kennedy, R. C.: J Endocr, 40, (1968): 371-381.

61. Liggins, G. C., And Grieves, S.: Possible role for prostaglandin F 2 alpha in parturition in sheep. Nature (London), 232, (1971): 629.

62. Lindholm, J. and Schultz-Moller, N.: Plasma and urinary cortisol in pregnancy and during estrogen-gestage treatment. Scand J of Clin and Lab Investigation, 31, (1973): 119-122.

63. Lindner, H. R.;:Blood cortisol in sheep: normal concentration and changes in ketosis of pregnancy. Nature (London), 184, (1959): 1645-1646.

64. Lindner, H. R.: J Endocr, 28, (1964): 301.

65. Lindner, H. R., Sass, M. B. and Morris, B.: Steroid in the ovarian lymph and blood of concious ewes. J Endocr, 30, 361-376.

66. Macleod, N. S. M., and Watt, J. A.: Listeria monocytogenes type 5 as a cause of abortion in sheep. Vet Record, 95, (1974): 365-367.

67. McGracken, J. A., Uno, A., Goding, J. R., Ichikawa, Y., and Baird, D. T.: The in vivo effects of sheep pituitary gonadotropins on the secretion of steroids by the autotransplanted ovary of the ewe. J Endocr, 45, (1969): 425-440.

68. McNatty, K. P., Thurley, D. C.: Variation in peripheral progesterone levels during the day at different stages of gestation in sheep. N Z J Ag Res, 17, (1974): 309-310.

69. Moore, N. W. and Rowson, L. E. A.: Maintenance of pregnancy in ovariectomized ewes by means of progesterone. Nature, 184, (1959): 1410.

70. Neher, G. M. and Zarrow, M.: Concentration of progestin in the serum of the non-pregnant, pregnant and post-partum ewe. J Endocr, 11, (1954): 323-330.

71. Niswender, G. D., Roche, J. F., Foster, D. L., Midgley, A. R. Jr.: Radioimmunoassay of serum levels of luteinizing hormone during the cycle and early pregnancy in ewes. Proc Sco Exp Biol Med, 129, (1968): 901-904.

72. Osburn, B. I., Stabenfeldt, G. H., and Ewing, L. L.: Relation of plasma progesterone to mid and late term bovine abortions due to Vibrio fetus infection. J Reprod Fert, 20, (1969): 77-82.

73. Paterson, J. Y. F., and Harrison, F. A.: The specific activity of plasma cortisol in sheep after intravenous infusion of $(1,2-{}^3H_2)$ cortisol and its relation to the distribution of cortisol. J Endocr, 40, (1968): 37-47.

74. Paterson, J. Y. F.: Biochem J, 86, (1963):1.

75. Paterson, J. Y. F., and Linzell, J. L.: Cortisol secretion rate, glucose entry rate and the mammary uptake of cortisol and glucose during pregnancy and lactation in dairy cows. J Endocr, 62, (1974): 371-383.

76. Rawlings, N. C., and Ward, W. R.: Endocrine changes in the ewe and her fetus correlated with uterine activity during parturition. J Reprod Fert, 31, (1972): 503-504.

77. Roberts, J. S., and Share, L.: Effects of progesterone and estrogen on blood levels of oxytocin during vaginal distention. Endocrinology, 84, (1969): 1076.

78, Robertson, H. A. and Sarda, I. R.: A very early pregnancy test for mammals: it application to the cow, ewe and sow. J Endocr, 49, (1971): 407-419.

79. Robertsson, H. A., and Smeaton, T. C.: The concentration of unconjugated oestrone, oestradiol-17-alpha and oestradiol-17-beta in the maternal plasma of the pregnant ewe in relation to the initiation of parturition and lactation. J Reprod Fert, (1973): 461-468.

80. Robertson, H. A.: Sequential changes in plasma progesterone in th

cow during the estrous cycle, pregnancy, at parturition, and post-partum. Can J Anim Sci, 52, (1972): 645-658.

81. Roux, Ch., Aubry, M. M., and Horvath, C.: AY-9944 induced abortion inhibited by progesterone. Tetralogy, 10, (1974): 321.

82. Scaramuzzi, R. J. Caldwell, B. V., and Moor, R. M.: Radioimmunoassay of LH and estrogen during the estrous cycle of the ewe. Biol Reprod, 3, (1970): 110-119.

83. Sarda, I. R., Robertson, H. A. and Smeaton, T. C.: Sequential changes in plasma progesterone levels in the ewe during the estrous cycle and during pregnancy in intact and ovariectomized sheep. Can J Anim Sci, 53, (1973): 25-34.

84. Seamark, R. F.: Presiding over steroids and reproduction session, In; J Reprod Fert, 24, (1971): 146.

85. Short, R. V.: Progesterone in blood. II. Progesterone in the peripheral blood of pregnant cows. J Endocr, 16, (1958): 426.

86. Short, R. V., and Moore, N. W. Progesterone in blood. V. Progesterone and 20 alpha-hydroxy-pregn-4-eh-3-one in the placenta and blood of ewes. J Endocr, 19, (1959): 288-293.

87. Short, R. V., McDonald, M. F., and Rowson, L. E. A.: Steroids in the ovarian venous blood of ewes before and after gonadotrophic stimulation. J Endocr, 26, (1963): 155-169.

88. Simmer, H, H., Tulchinsky, D., Gold, E. M., Frankland, M., Greipel, M., and Gold, A. S.: On the regulation of estrogen production by cortisol and ACTH in human pregnancy at term. Am J Obstet Gyn, 119, (1974): 283-296.

89. Smith, I. D. and Hughes, K. L.: Progesterone concentrations in the peripheral plasma of pregnant ewes following infection with an abortifacient organism. Res in Vet Sci, 16, (1974): 116-118.

90. Spears, L. L. Bercovita, A. B., Reynolds, W. L., Kreider, J. L., and Godke, R. A.: Induction of parturition in beef cattle with estradiol and PGF 2 alpha. J Ani Sci, 39, (1974): 227.

91. Speroff, L., and Ramwell, P. W.: Prostaglandins in reproductive physiology. Am J Obstet Gyn, 108, (1970): 1111.

92. Stabenfeldt, G. H., Drost, M., and Beames, C.: Plasma progesterone levels during pregnancy. Fed Proc, 29, (1970): 706.

93. Stormshak, F., Kelly, H. E., and Hawk, H. W.: Suppression of ovine luteal function by 17 beta oestradiol. J Endocr, 45, (1969): 425-440.

94. Strott, C. A., Sundel, H., and Stahlman, M. T.: Maternal and fetal plasma progesterone, cortisol, testosterone and 17-beta-estradiol in preparturient sheep: response to fetal ACTH infusion. Endocrinology, 95, (1974): 1327-1339.

95. Tescher, M., Morin, P., Astier, A., Techenet, J., Engelmann, P., and Dieulangard, P.: Cortisolemie et grossesse. Sem Hop Paris (1974): 1341-1347.

96. Tescher, M., Morin, P., and Engelmann, P.: Glyco-regulation hormonale pendant la grossesse. correlations entre insuline, cortisol et H.C.S. Sem Hop Paris (1974): 1349-1358.

97. Thompson, F. N., and Wagner, W. C.: Fetal-maternal corticosteroid relationships in sheep during late pregnancy. J Reprod Fert, 41, (1974): 49-56.

98. Thompson, F. N., and Wagner, W. C.: Plasma progesterone and oestrogens in sheep during late pregnancy: contribution of the maternal adrenal and ovary. J Reprod Fert, 41, (1974): 50-66.

99. Thorburn, G. D., Nicol, Diane H., Bassett, J. M., Shutt, D. A. and Cox, R. I.: Parturition in the goat and sheep: changes in corticosteroids, progesterone, oestrogens and prostaglandin.F. J Reprod Fert, 16, (1972): 61-84.

100. Thorburn, G. D. and Schneider, W.; The progesterone concentration in the plasma of the goat during the oestrus cycle and pregnancy. J Endocr, 52, (1972): 23-26.

101. Tyack, A. J., Lambadarios, Carol, Parsons, R. J., Stewart, C. R., Cooke, I. D.: Plasma progesterone and oestradiol-17-beta changes during abortion induced by prostaglandin F 2 alpha. J Ob Gyn of the British Commonwealth, 81, (1974): 52-56.

102. Ward, H. Rochman, H., Varnavides, L. A., and Whyley, G. A.: Hormone and enzyme levels in normal and complicated pregnancy. Am J Ob Gyn, 116, (1973): 1105-1113.

103. Widholm, O., Kajanoja, P. and Johansson, E. D. B.: Serum levels of oestradiol and progesterone during administration of prostaglandin F 2 alpha for induction of abortion and labour. Acta Ob Gyn Scand, 54, (1975): 135-139.

THIS BOOK CONTAINS NUMEROUS PAGES WITH DIAGRAMS THAT ARE CROOKED COMPARED TO THE REST OF THE INFORMATION ON THE PAGE.

THIS IS AS RECEIVED FROM CUSTOMER.

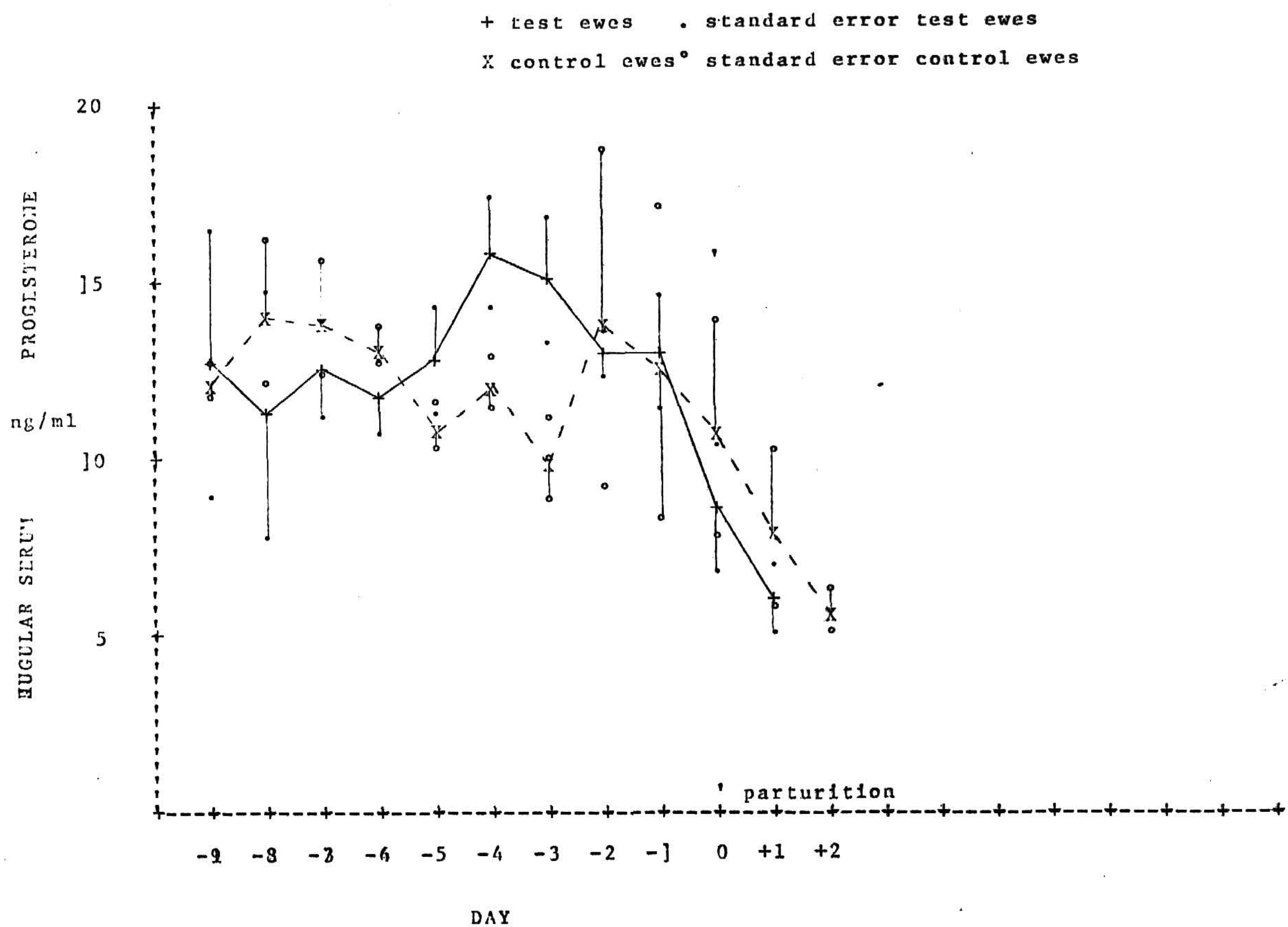
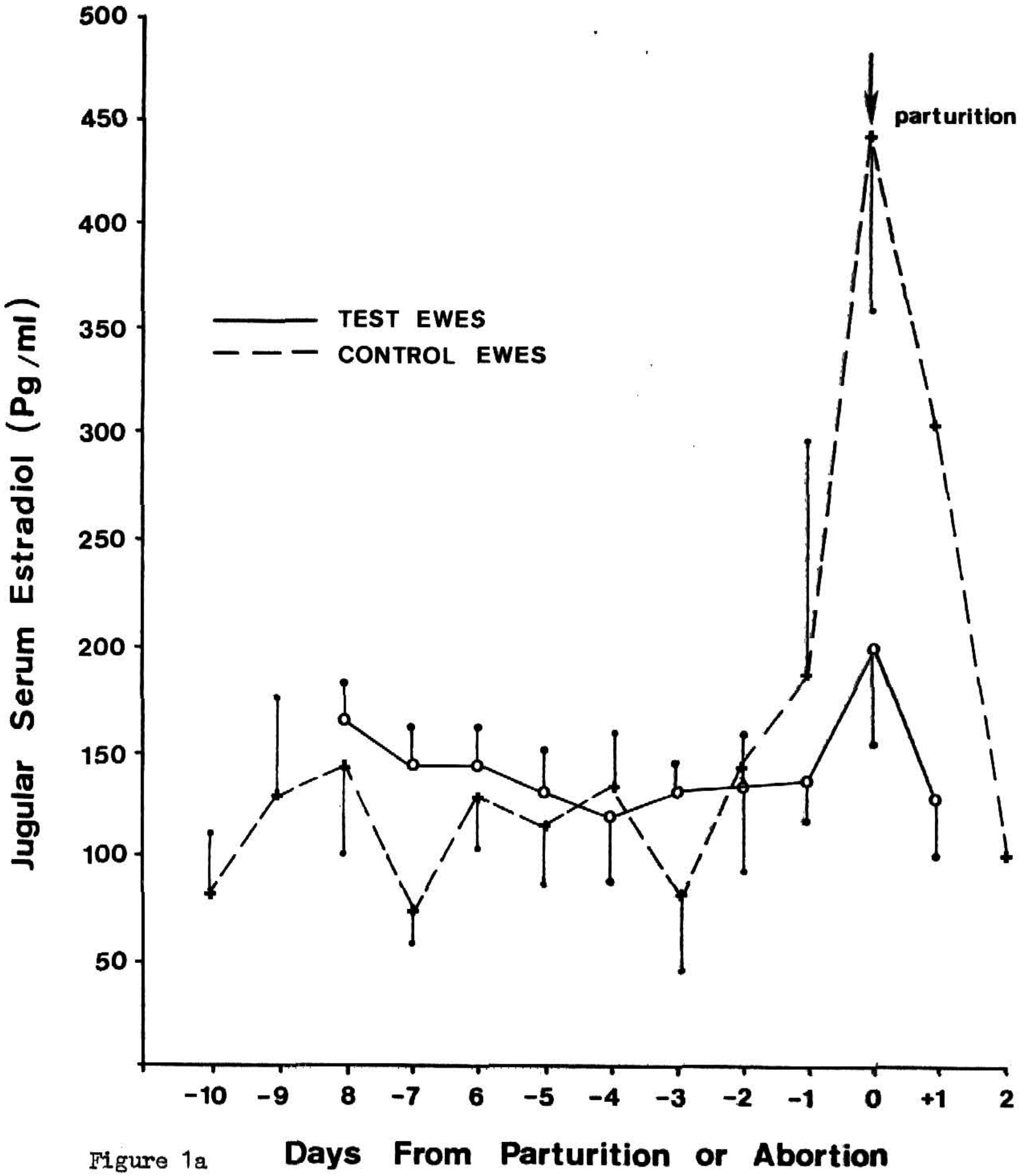


Figure 1. Serum levels of progesterone in 4 normal pregnant ewes and 12 pregnant ewes receiving Listeria monocytogenes, day 0 normalized to day of parturition or abortion. Vertical bars inidicate the standard error of the means.



Jugular Serum Estradiol (Pg/ml)
500
450
400
350
300
250
200
150
100
50
TEST EWES
CONTROL EWES
parturition
-10 -9 8 -7 6 -5 -4 -3 -2 -1 0 +1 2
Days From Parturition or Abortion

Figure 1a

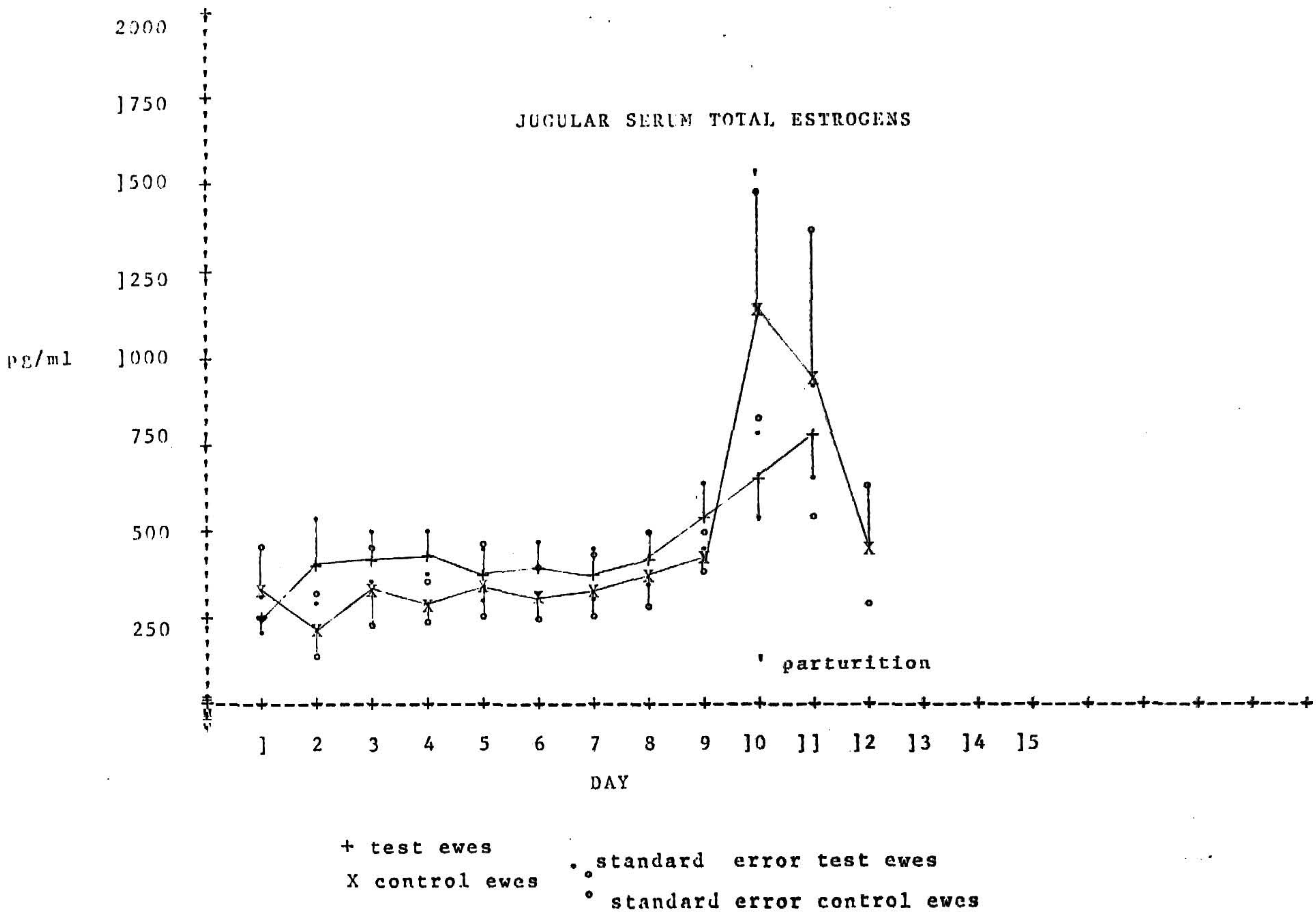


Figure 2. Serum levels of total estrogens in 4 normal pregnant ewes and 12 pregnant ewes receiving Listeria monocytogenes, day 0 normalized to day of parturition or abortion.

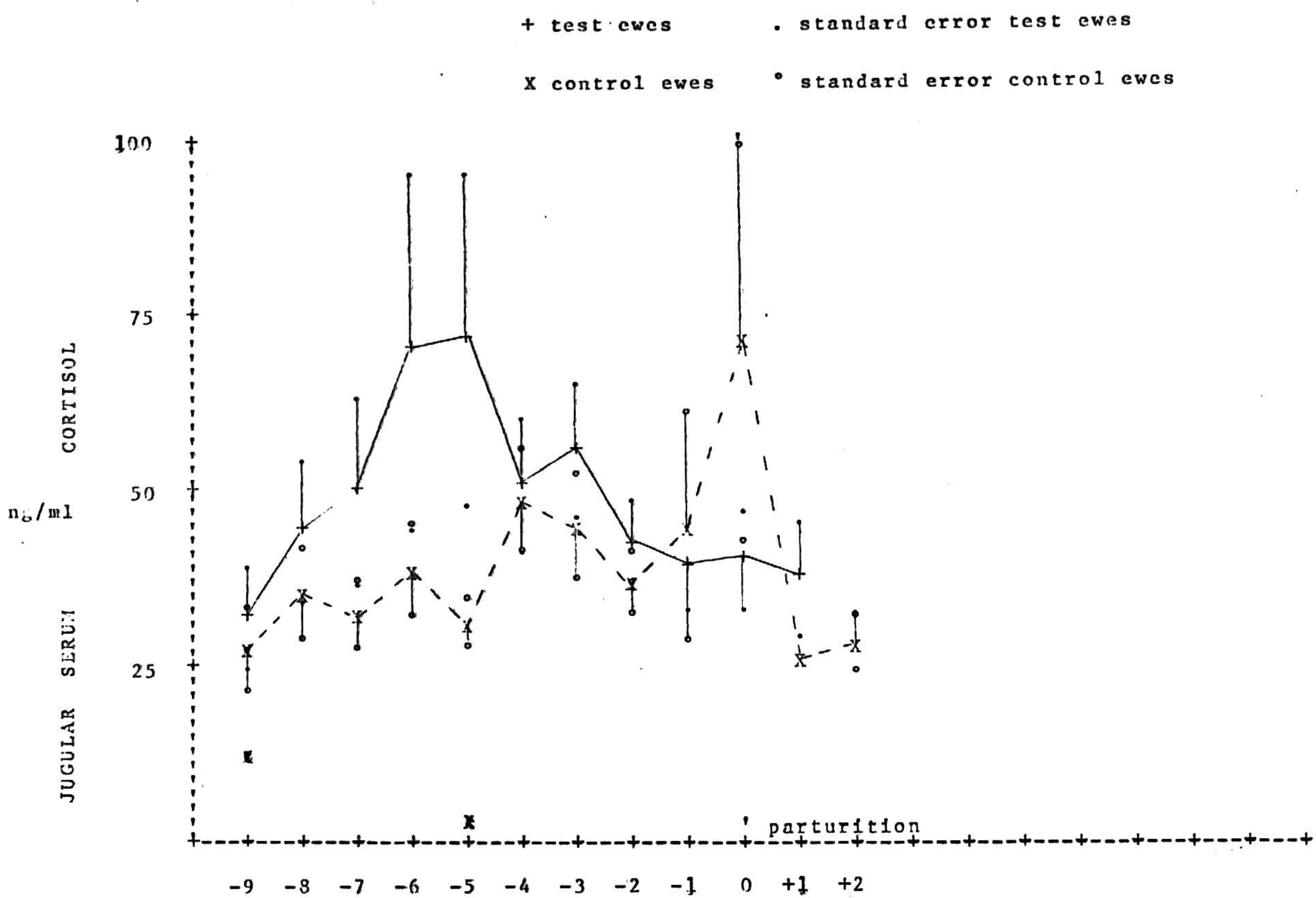


Figure 3. Serum levels of cortisol in 4 normal pregnant ewes and 12 pregnant ewes receiving Listeria monocytogenes, day 0 normalized to day of parturition or abortion. Vertical bars indicate the standard error of the means.

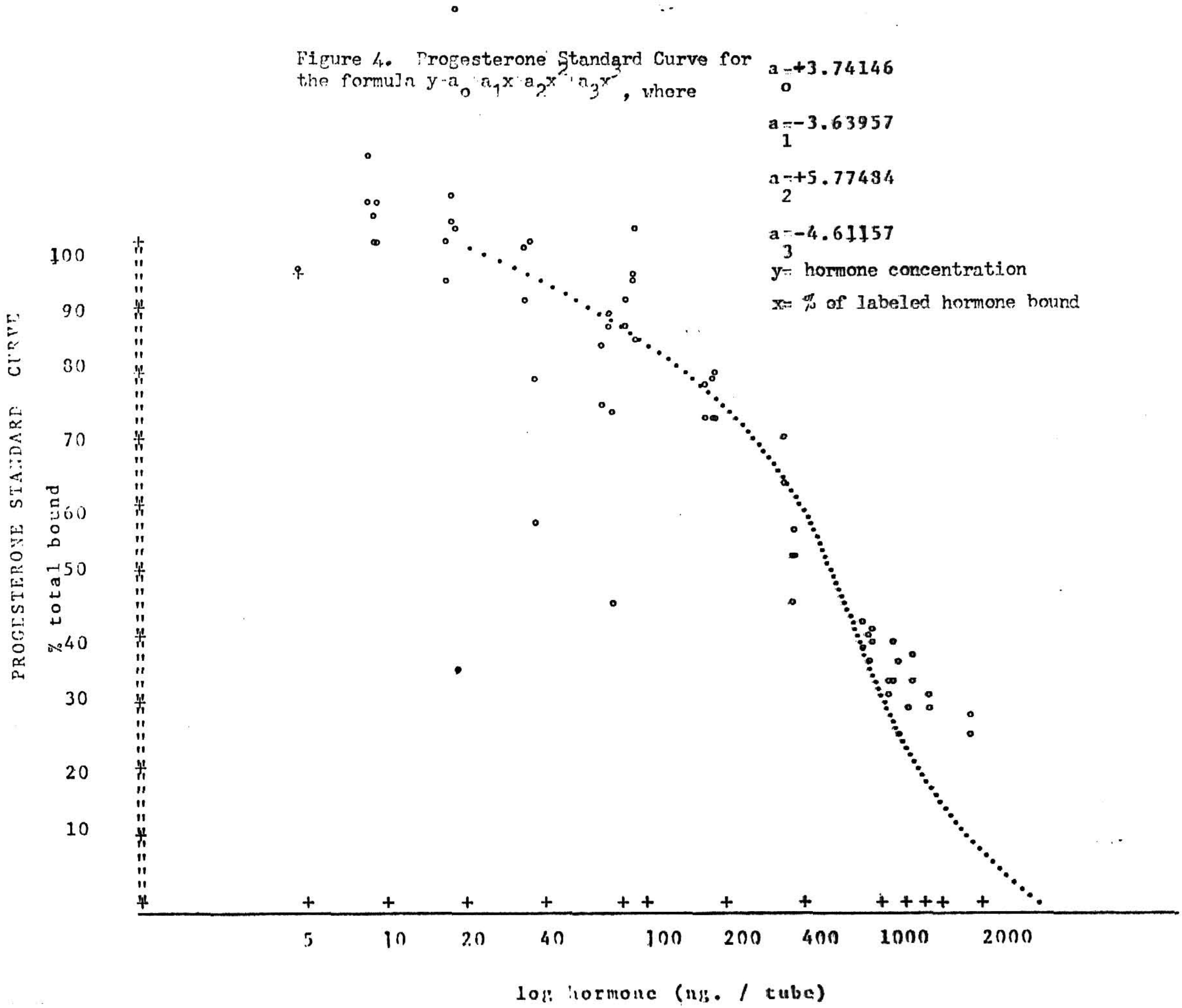


Figure 4. Progesterone Standard Curve for the formula $y = a_0 + a_1x + a_2x^2 + a_3x^3$, where

$a_0 = +3.74146$

$a_1 = -3.63957$

$a_2 = +5.77484$

$a_3 = -4.61157$

y = hormone concentration

x = % of labeled hormone bound

Figure 5. Estrogen Standard Curve for the formula $y = a_o + a_1x + a_2x^2 + a_3x^3$, where,

$a_o = 3.54464$

$a_1 = -7.70948$

$a_2 = 14.60744$

$a_3 = -9.63126$

y ± hormone concentration

x - % of labeled hormone bound

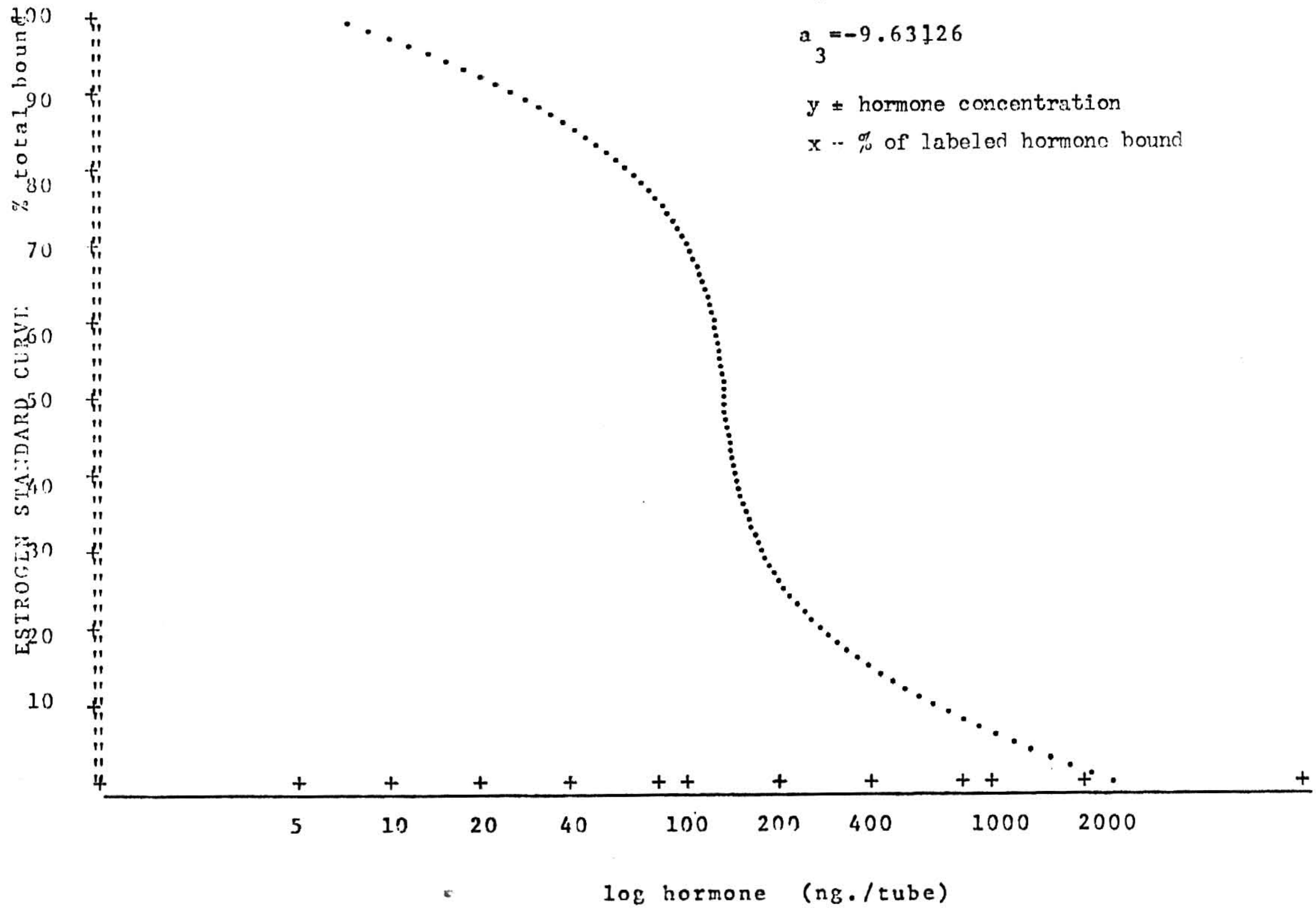
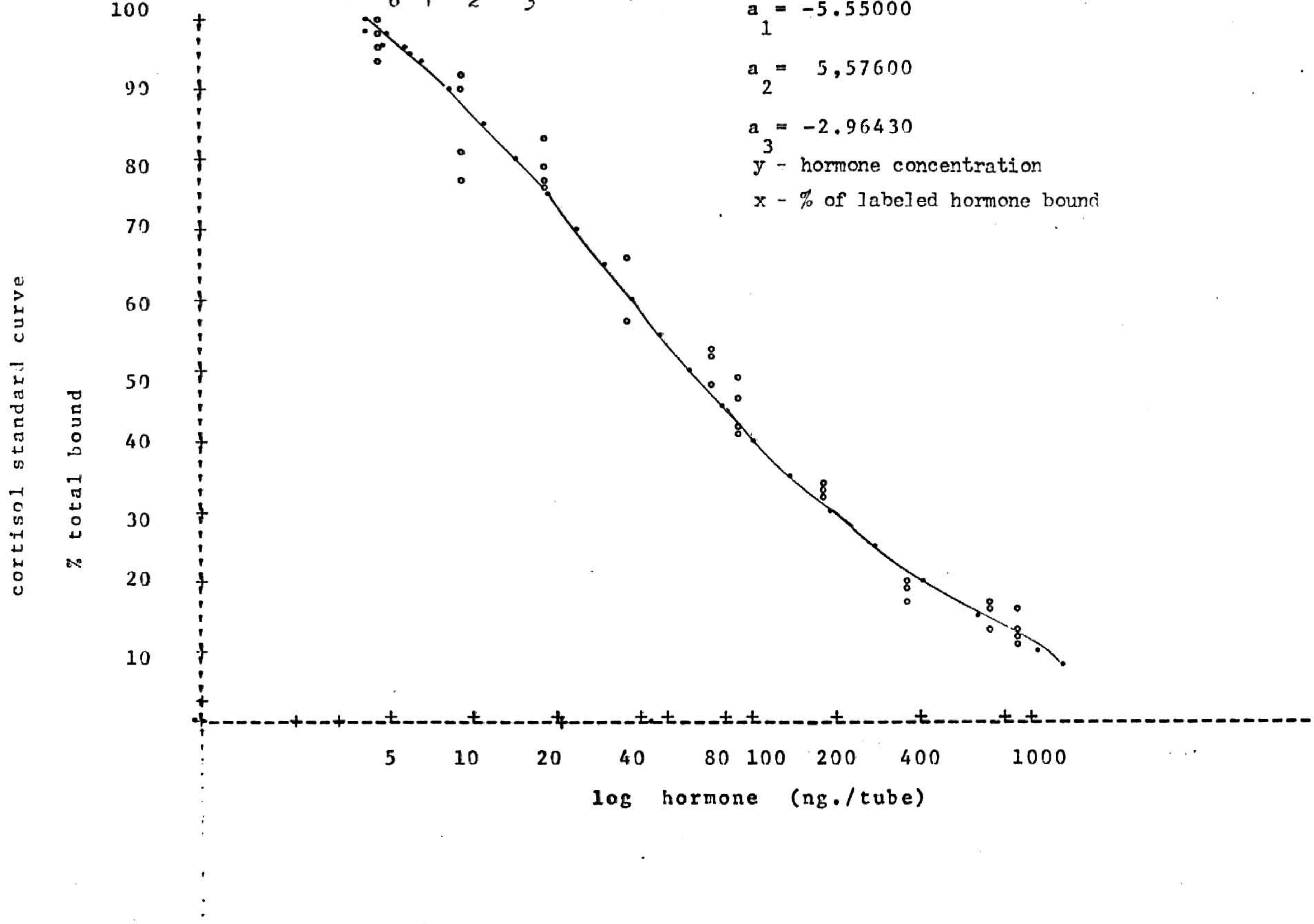


Figure 6. Cortisol Standard Curve for the formula $y = a_o + a_1x + a_2x^2 + a_3x^3$ where,



III. CLINICAL-PATHOLOGICAL CHANGES IN THE SERUM OF EWES ABORTING DUE TO *LISTERIA MONOCYTOGENES*.

Introduction

Both parturition and abortion are complex physiological processes. Some of the clinical-pathological changes occurring at parturition have been reported. A decrease in the serum calcium has been observed in cattle [22]. Studies have shown an increase in serum glucose in sheep [3] and goats [23] at parturition, but no increase was observed in another study in sheep [11]. Hypercholesterolemia was observed in pregnant women up to the 33rd week of pregnancy [15]. A decline in total protein (TP) in goats has been reported at parturition and continuing for 8 days post-partum [23], and little change was observed in the packed cell volume (PCV) during or after labour in sheep [3]. Alkaline phosphatase (AP) and lactic dehydrogenase (LDH) have been measured in humans with abnormal pregnancys. The studies on AP showed poor correlation between alkaline phosphatase levels and complications occurring during pregnancy [24,16]. An increase in LDH in human amniotic fluid has been reported following fetal death and the changes in the amniotic fluid were similar to the changes observed in the maternal serum [25].

Materials and Methods

Animals: Suffolk and crossbred ewes in the last third of gestation were selected as test and control animals. The ewes were housed indoors in a heat and light controlled enviroment. Twelve test ewes were each inoculated intravenously in the jugular vein with 5 ml. of six hour broth culture of Listeria monocytogenes. Four control ewes were each inoculated with 5 ml. of the broth medium. Five ml. of whole blood were collected daily by venapuncture of the jugular veins. The serum was drawn off into culture tubes and frozen. Two additional ml. of blood was collected daily with heparin as an anticoagulant.

Assay: Serum samples were analyzed for calcium, phosphorous, glucose, albumin, TP, AP, cholesterol, total bilirubin, LDH, serum glutamic-oxalic transaminase (SGOT), uric acid and blood urea nitrogen (BUN) with an autoanalyzer (SMA 12). The red blood cell and white blood cell counts were determined by using a Coulter counter. One hundred white blood cells were identified on Modified Wright's stained smears. The hemoglobin concentrations were determined by a cyanomethemoglobin spectrophotometry method [4], and rectal temperatures were recorded twice daily.

Results

A decrease in serum calcium from 9 mg. % to 8 mg. % and an increase in serum phosphorous from 4.2 to 5.0 mg. % were noted in the controls on the first day post-partum. (Figures 7 and 8). This trend was reversed on the second post-partum as the serum calcium increased from 8 to 10 mg. %, and the serum phosphorous decreased from 5 to 4.5 mg. %. No changes were observed in the test ewes. An increase in serum glucose from 70 to 100 mg. % was observed in the control ewes after delivery. (Figure 9) The serum levels of AP increased on the day of parturition in the test ewes from 11 to 13.5 King Armstrong Units (KAU). (Figure10) The serum AP in the control ewes decreased from 13.5 to 12 KAU on the day after parturition. In the controls the serum cholesterol gradually decreased from a peak value of 68 mg. % on the sixth day pre-partum to 59 mg. % on the first day post-partum, and then increased to 62 mg. % on the second day post-partum. (Figure 11) The test ewes had consistently higher levels of total bilirubin (Figure 12), LDH (Figure 13), and SGOT (Figure 14) than the controls, but the controls had higher levels of uric acid. (Figure 15) A temperature rise to 104.2 F occurred in the test ewes on the second day post-inoculation. (Figure 16) The white cell numbers were increased after inoculation of the test ewes from 10,000 per ml. to 13,000 per ml., with an increase in the percentage of neutrophils after inoculation and at abortion. (Figure 17) No significant changes were noted in serum albumin and BUN. The PCV, hemoglobin concentration and red blood cell counts showed no pattern.

Discussion

The major changes observed were the changes in the calcium, phosphorous, and glucose levels and in the rectal temperatures. The other parameters showed only slight changes which were not stastically significant. The drop in serum calcium occurring at parturition in the controls was similar to changes reported in cattle [22]. The decrease in calcium and corresponding increase in phosphorous on the first day post-partum may have been due to an increased release of thyrocalcitonin. The increase in serum calcium and decrease in serum phosphorous on the second day post-partum is compatible with a compensatory reaction of parathormone. No changes in serum calcium or phosphorous were observed in test ewes which aborted prior to term. This could be due to a lack of milk production.

An increase in maternal serum glucose at birth siminlar to the increase seen in the control ewes has been reported in sheep [3] and in goats [23], but in another study using sheep no increase was observed [11]. An increased release of adrenaline, glucocorticoids and/or glucagon could be responsible for the increase in the maternal serum glucose of the controls at parturition. Other reports indicate that these compounds could be increased at parturition [3,7,23]. The serum glucose of both the test and control ewes coincided closely with their cortisol levels. The post-inoculation hyperglycemia of the test ewes could be secondary to the release of these factors with the lack of response of the test ewes at abortion due to exhaustion of the supplies of these compounds.

The changes seen in AP in this study could have been due to changes in liver, intestine, bone and/or the placenta [14], and it was difficult to draw conclusions from these changes.

No hypercholesterolemia as has been observed in human beings [15], was observed in either the test or control ewes. The values observed ranged from 55 to 70 mg. %, which is comparable to the normal values seen in sheep [12].

The increased levels of LDH, SGOT, and total bilirubin in the test ewes may indicate the possibility of either maternal or fetal tissue damage. An increase in LDH was recorded in human beings and was considered to be due to leakage from autolysed fetal tissue [22]. However, in this study using sheep the levels of maternal LDH in the test ewes was only slightly higher than the controls at parturition. No decrease in TT was seen in either the test or control ewes post-partum as has been reported in goats [23].

The temperature rise, increase in total white blood cell count and in percentage neutrophils coincide with the period of post-infection reaction. No significant changes were observed in the PCV, which is consistent with another report [3]. The serum albumin, serum BUN, hemoglobin concentration and red blood cell numbers also showed no pattern.

The major differences observed between the test ewes and the controls in the study appeared to be related to changes in function of the adrenal gland and perhaps the parafollicular cells of the thyroid gland. Both of these tissues appeared hypoactive at abortion of the test ewes.

Summary

Clinical-pathological changes were measured in pregnant ewes infected with *Listeria monocytogenes* and in normal control ewes at abortion or parturition. Rectal temperatures were also taken. The major changes observed were the changes in the calcium, phosphorous, and glucose levels and in the rectal temperatures. The other parameters showed only slight changes which were not stastically significant.

A decrease in serum calcium and an increase in serum phosphorous were noted in the control ewes at 1 day post-partum. An increase in glucose was observed in the control ewes following delivery. The serum alkaline phosphatase rose on the day of parturition in the test ewes, but the alkaline phosphatase of the controls did not increase and decreased the day after parturition to below pre-parturition levels. Cholesterol gradually decreased in the controls until two days post-partum and then increased. The test ewes had consistently higher levels of total bilirubin, lactic dehydrogenase (LDH), and serum glutamic oxalic transaminase (SGOT) than the controls, but the controls had higher levels of uric acid. A temperature rise occurred in all of the test ewes after inoculation. The white blood cell counts were increased after inoculation in the test ewes, with an increase in the percentage of neutrophils after inoculation and at abortion. No significant changes were noted in serum albumin and serum blood urea nitrogen (BUN). The packed cell volume, hemoglobin concentration and red blood cell numbers showed no pattern.

REFERENCES

1. Care, A. D., Pickard, D. W., Garel, J. M., Barlet, J. P., Tomlinson, S., and O'Riordan, J. L. H.: Autonomy of calcium homeostasis in the sheep foetus. Horm Metab Res, 7, (1975): 103.

2. Caspi, E., Rachmani, P., Pinto, N., Zaidman, J. L.: Serum alkaline phosphatase in normal and pathological pregnancy. Israel J Med Sci, 9, (1973): 557-558.

3. Comline, R. S., Silver, Marian: The composition of foetal and maternal blood during parturition in the ewe. J Physiol, 222, (1972): 233-256.

4. Crosby, W. H., Munn, J. I. and Furth, F. W.: Standardizing a method for clinical hemoglobinometry. U. S. Armed Forces Med J, 5, (1954): 693.

5. Duggin, G. C., Lyneham, R. C., Dale, Nancy E., Evans, R. A., and Tiller, D. J.: Calcium balance in pregnancy. The Lancet, II, 7886, (1974): 926-927.

6. Duggin, G. C., Lyneham, R. C., Dale, Nancy E., Evans, R. A. and Tiller, D. J.: Calcium balance in pregnancy. The Lancet, I, 7897, (1975): 36.

7. Harper, H. A.: Review of Physiological Chemistry. 13th ed. Lange Medical Publication, Maruzen Company Ltd. (1971).

8. Hytten, F. E., Lind, T., Thomson, A. M.: Calcium balance in pregnancy. The Lancet, II, 7889, (1974): 1152.

9. Kinney, J. M.: Br J Surg, 54, (1967): 127.

10. Labow, R. S., Williamson, D. G., and Layne, D. S.: The transfer of glucose to steroids by sheep liver microsomes. Can J Biochem, 52, (1974): 203-207.

11. Mellor, D. J., and Slater, J.S.: Variations in the distribution of glucose and fructose within chronically catherized sheep conceptuses during the last two months of pregnancy. Res Vet Sci, 15, (1973): 317-321.

12. Morris, B., and Courtice, F. C.: The protein and lipid composition of the plasma of different animal species determine by zone electrophoresis and chemical analysis. Quart J Exp Physiol, 40, (1955): 127.

13. Morriss, F. H. jr., Rosenfeld, C. R., Resnik, R., Meschia, G., Makowski, E. L. and Battaglia F. C.: Growth of uterine oxygen and glucose uptakes during pregnancy in sheep. Gyn Invest, 5, (1974): 230-241.

14. Okuno, R., and Freud, W.: Albumin preparations and placental alkaline phosphatase activity. Transfusion, 13, (1973): 19-22.

15. Oliver, M. F. and Boyd, G. S.: Clin Sci, 14, (1955): 15.

16. Oram, R. H., and Gane, M. F. E.: Doubts on the value of serum heat-stable alkaline phosphatase estimations in pregnancy. S AFR Med J 47, (1972): 2017-2018.

17. Owen, V. M. J., Ho, F. F. K.,Mazzuchin, A., Doran, T. A., Leidgren, S., and Porter, C. J.: The determination of cholesterol in amniotic fluid. Clin Chem, 20, (1974):906.

18. Ross, P. E., Coutts, J. R. T.and Macnaughton, M. C.: Free cholesterol levels in plasma from the maternal placental and fetal circulations duringbhuman pregnancy. Clinica Chimica Acta, 49, (1973): 415-422.

19. Sykes, A. R., and Field, A. C.: Effects of dietary deficiencies of energy, protein and calcium on the pregnant ewe IV. Serum total protein, albumin, globulin, transferrin and plasma urea levels. J Agric Sci Camb, 80, (1973): 29-36.

20. Telegdy, G., Robin, M., and Diczfalusy, E.: Quantitative assessment of the principal steroids formed by human placentas perfused with labelled cholesterol in vitro. Acta Endocrinologica, 72, (1973): 127-136.

21. Van Julsingha, E. B.: Prediction of outcome of pregnancy on the basis of SGOT and SGPT activities on day 19 of pregnancy of rabbits dosed with Org OD 14. Teratology, 8, (1973): 224.

22. Vercellotti, J. R., Barnett, L. B. and Gragle, R. G.: Levels of serum alpha-2-macroglobulin and calcium in the parturient cow. Federation Pro, 32, (1972): 908.

23. Verma, S. K., and Tyagi, R. P. S.: The effect of caesarian section and normal parturition upon the concentraion of blood electrolytes, glucose and total protein in goats. Res Vet Sci, 16, (1974): 162-166.

24. Ward, H., Rochman, H., Varnavides, L. A., and Whyley, G. A.: Hormone and enzyme levels in normal and complicated pregnancy. Am J Obst Gyn, 116, (1973): 1105-1113.

25. Ylostalo, P., Reinila, M., Raunio, V., and Jarvinen, P. S.: LDH and LDH isoenzymes in amniotic fluid in normal and complicated pregnancy. Annales Chirurgie et Gynaecologie Fenniae, 61, (1972): 206-210.

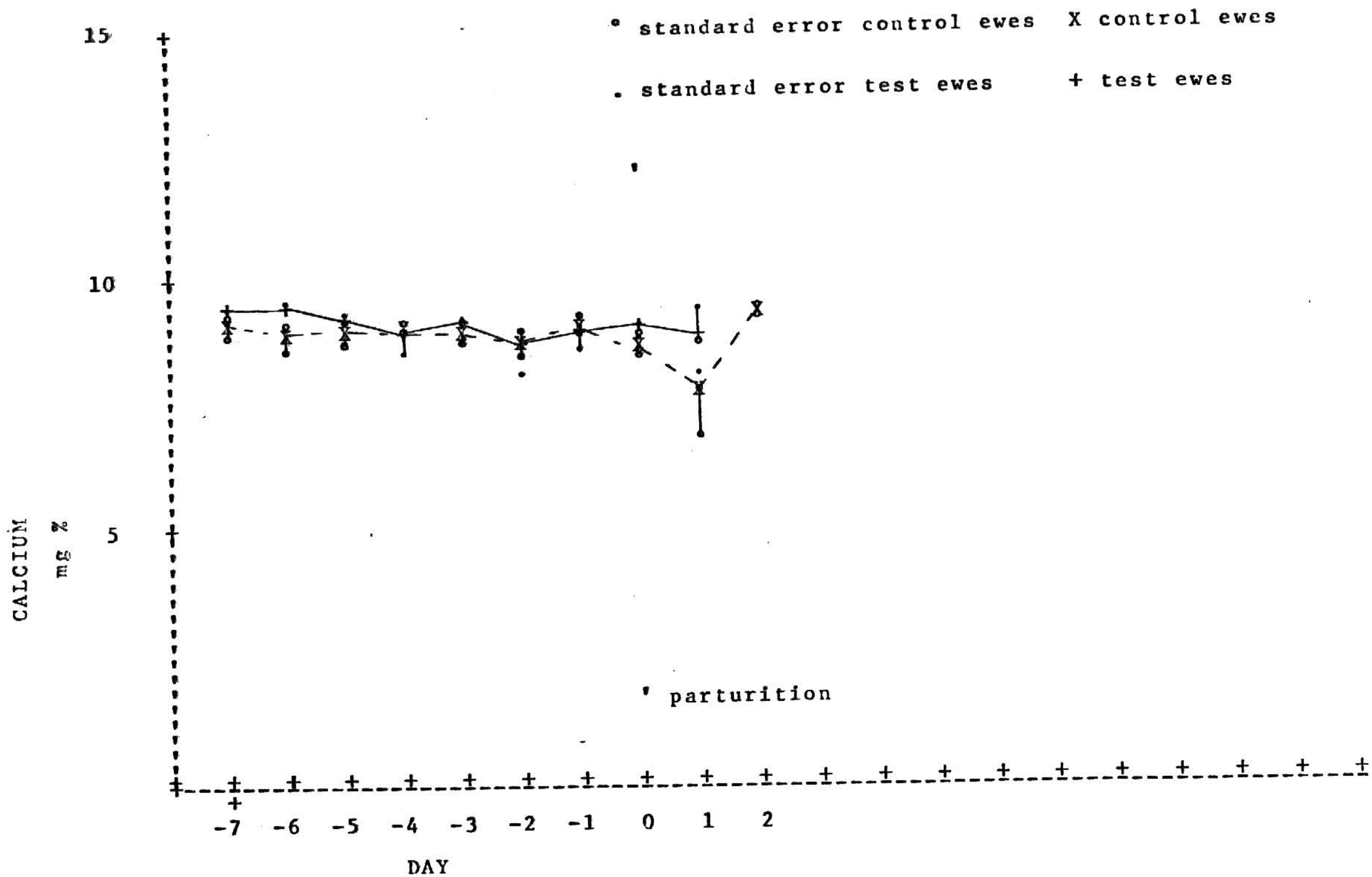


Figure 7. Serum calcium levels forcontrol pregnant ewes prior to and post-partum, test ewe data included for comparison, Day 0 normalized for parturition. The vertical bars represent standard error of the means.

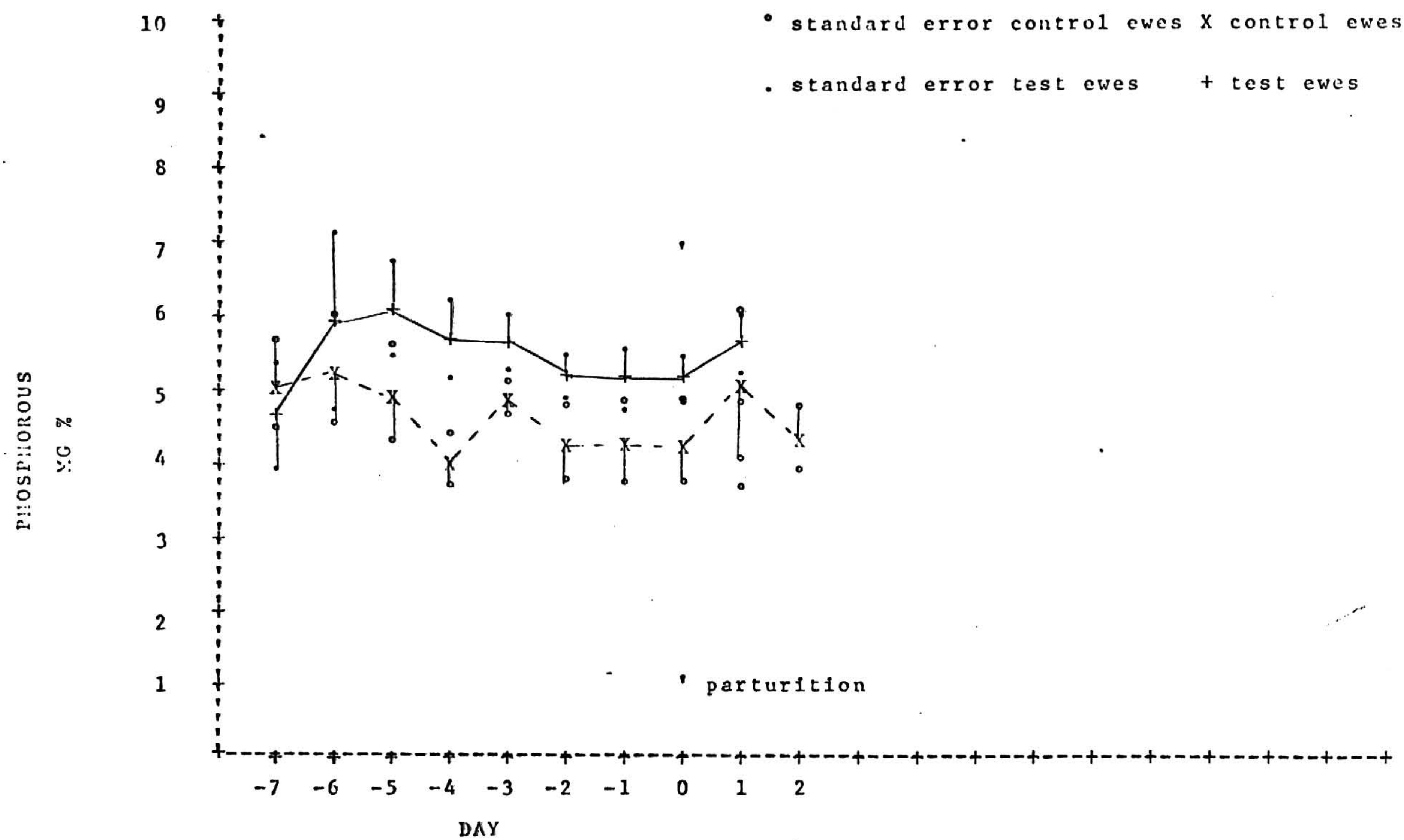


Figure 8. Serum phosphorous levels for control pregnant ewes prior to and post-partum, test ewe data included for comparison, Day 0 normalized for parturition. The vertical bars represent standard error of the means.

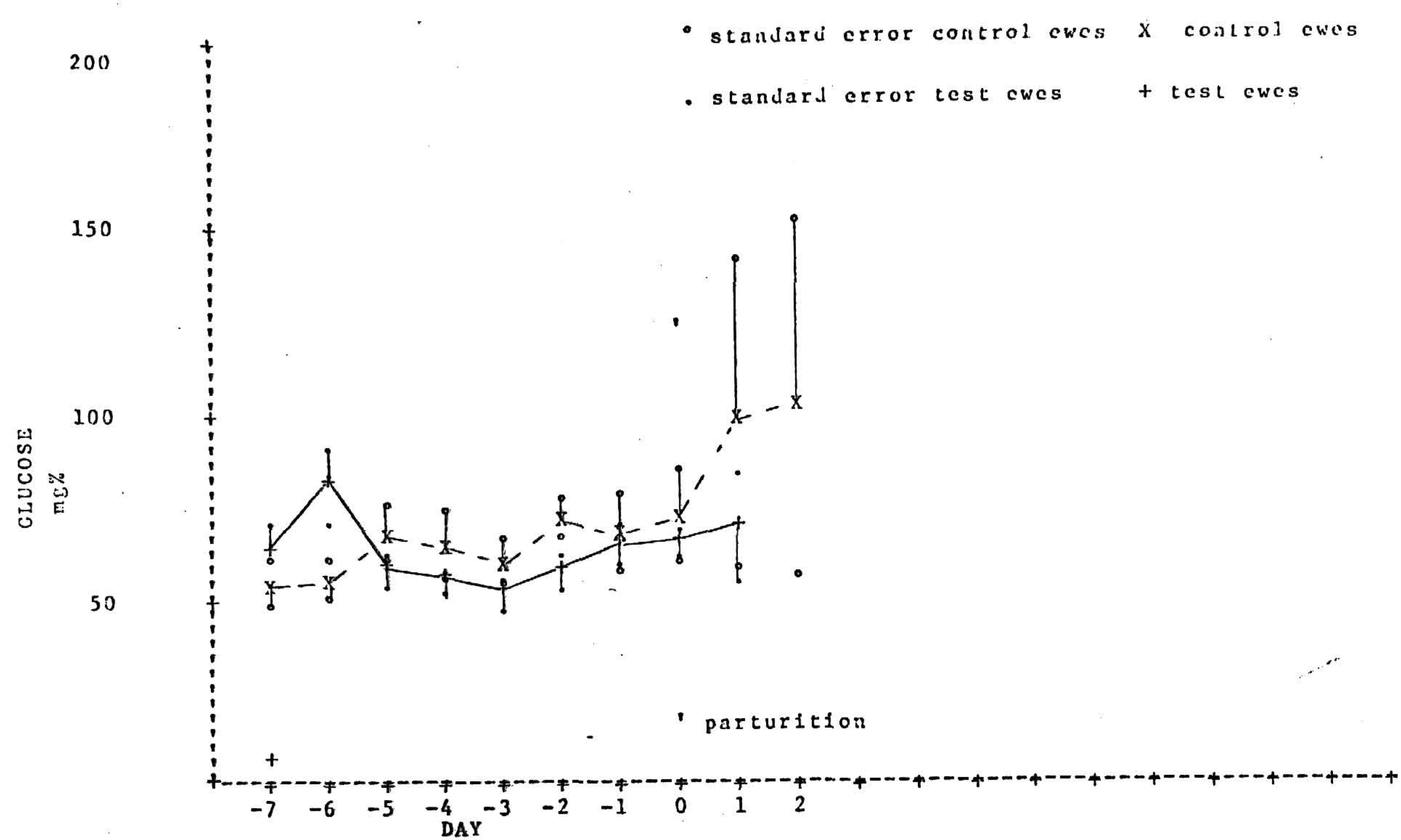


Figure 9. Serum glucose levels for control pregnant ewes prior to and post-partum, test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error ofthe means.

THIS BOOK WAS BOUND WITHOUT PAGE 54.

THIS IS AS RECEIVED FROM CUSTOMER.

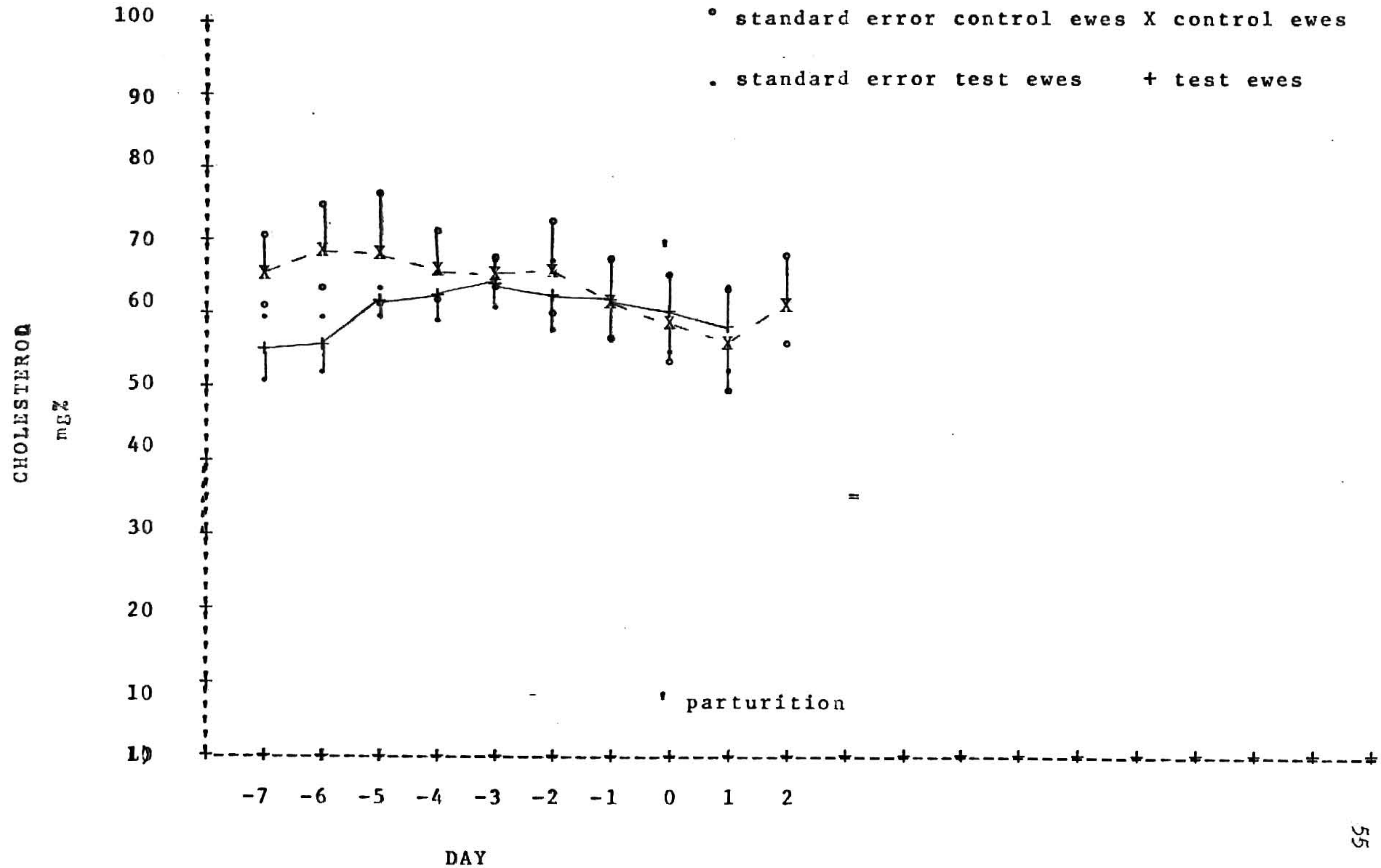


Figure 11. Serum cholesterol levels for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard errorof the means.

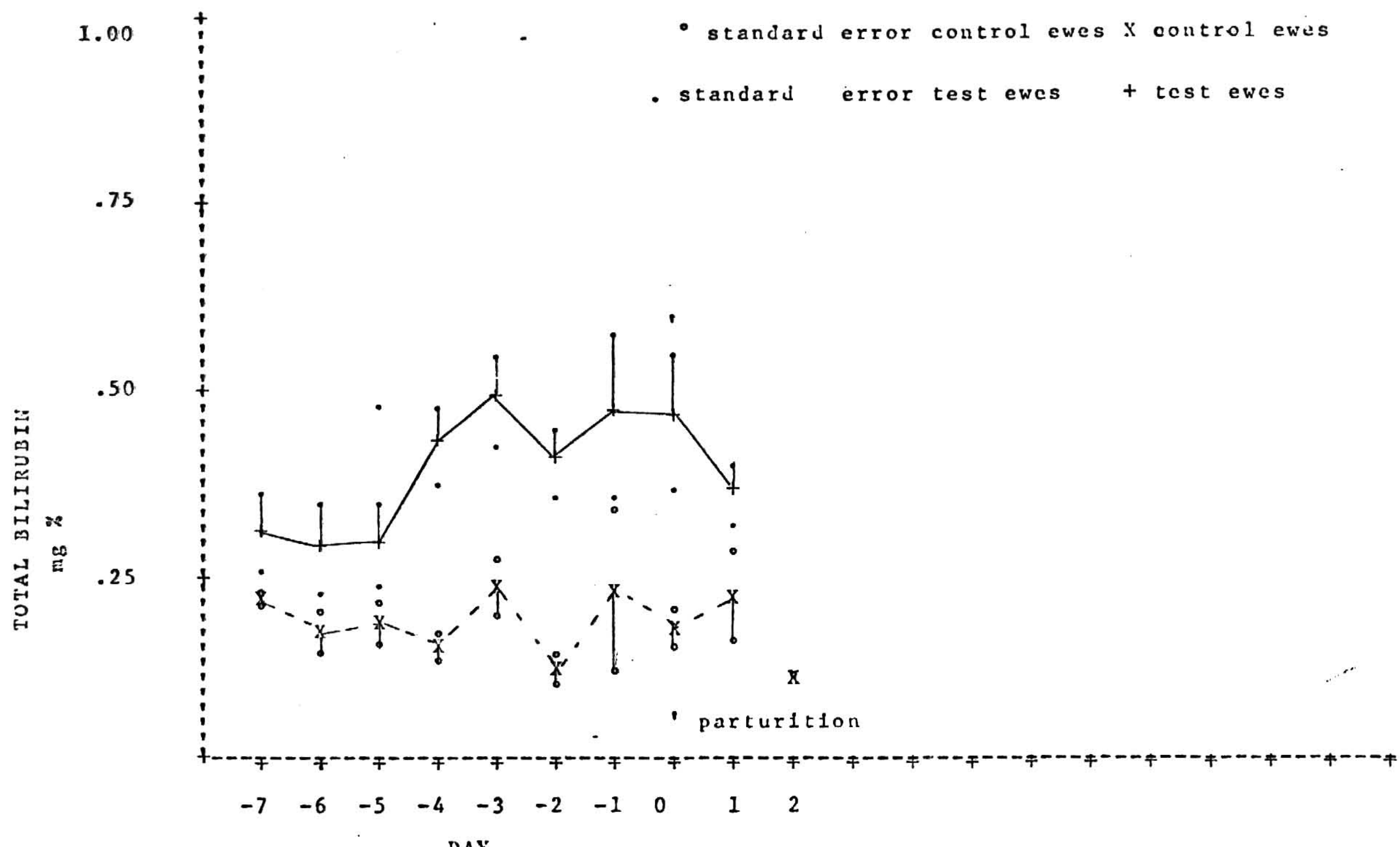


Figure 12 Serum total bilirubin levelsfor control pregnant ewes prior to and post-partum test ewe data included for comparison,day 0 normalized for parturition. The vertical bars represent standard error of the means.

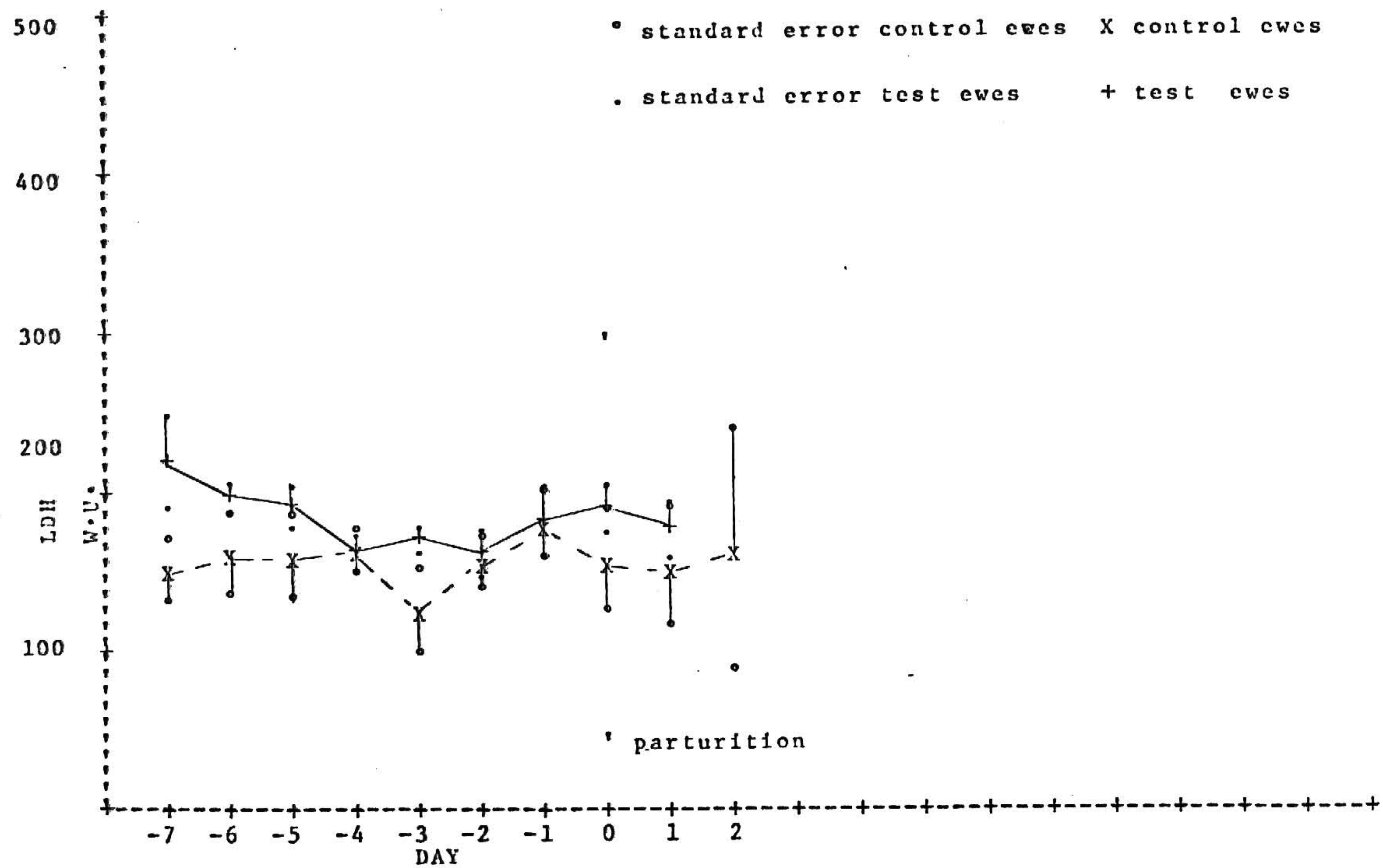


Figure 13. Serum lactic dehydrogenase levels for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

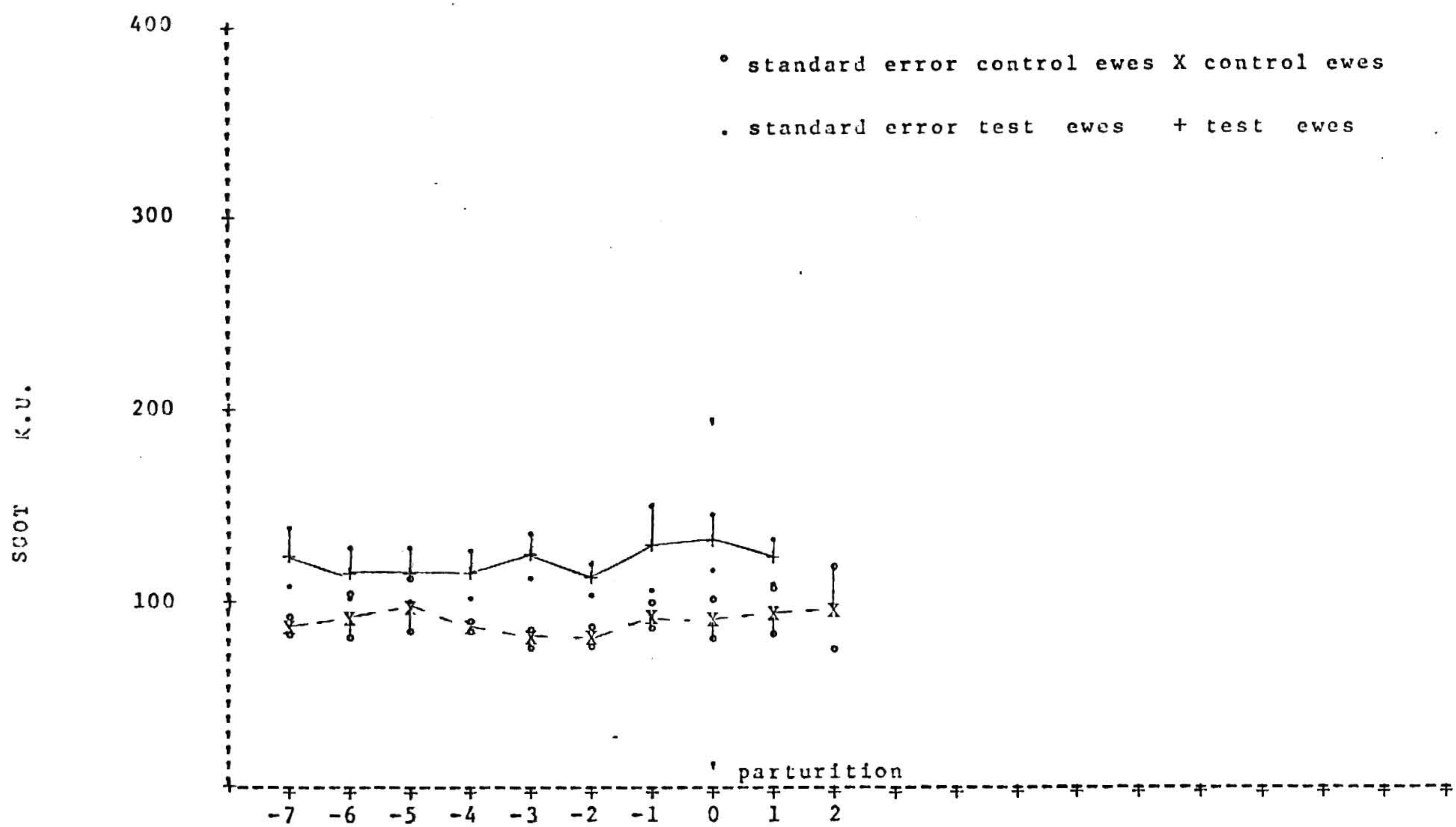


Figure 14. Serum SGOT levels for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

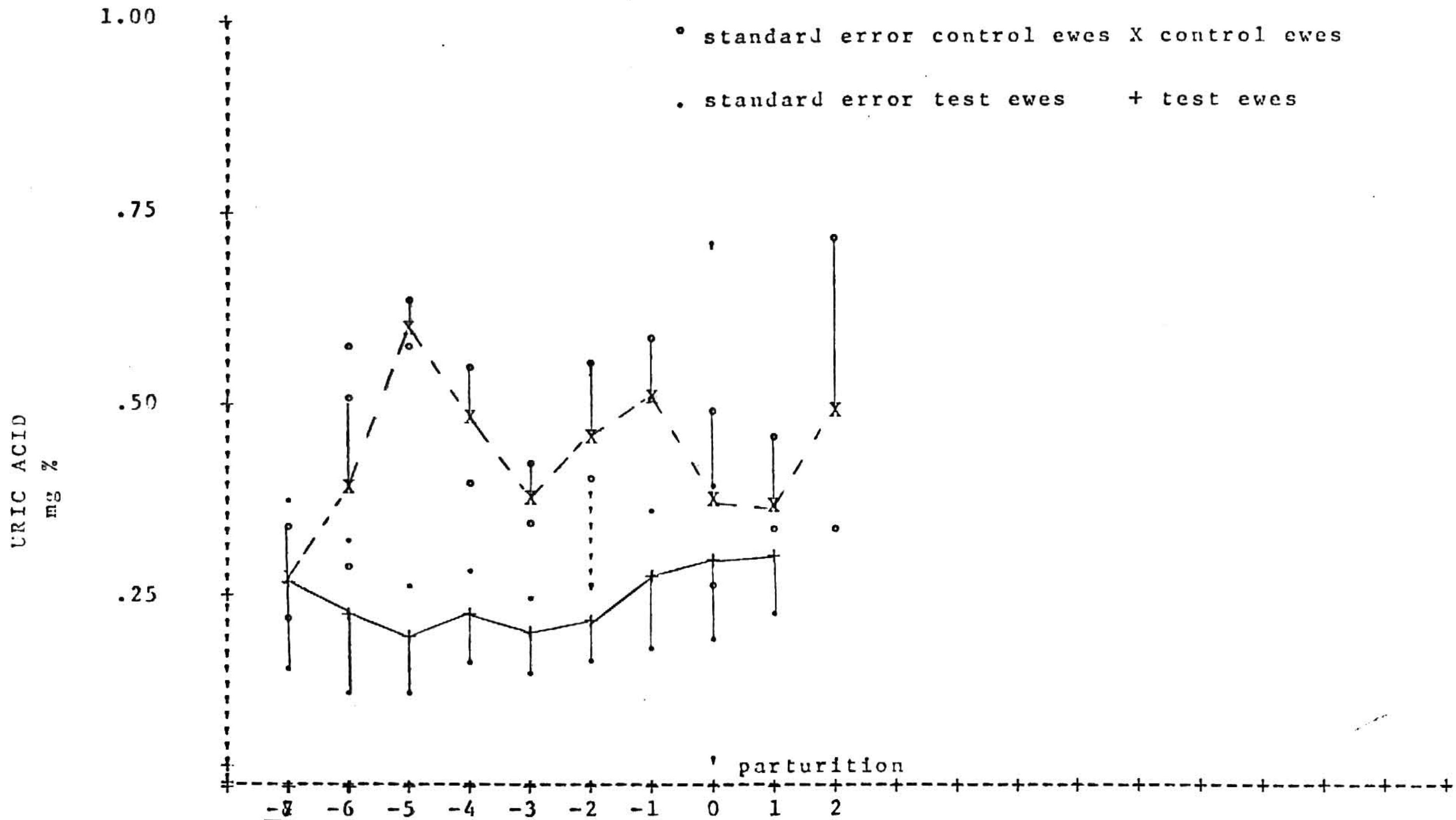


Figure 15 Serum uric acid levels for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

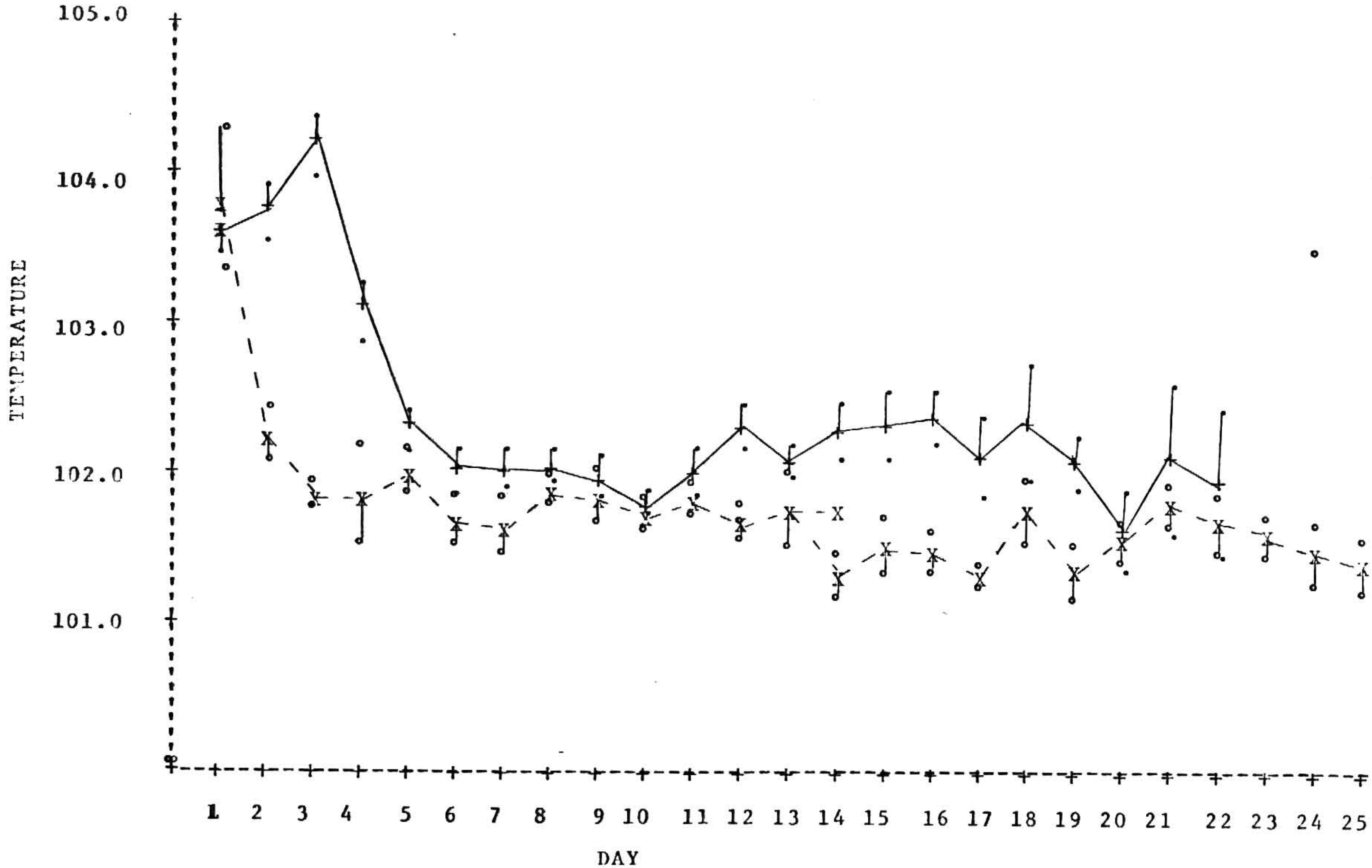


Figure 16. Temperature changes for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the maans.

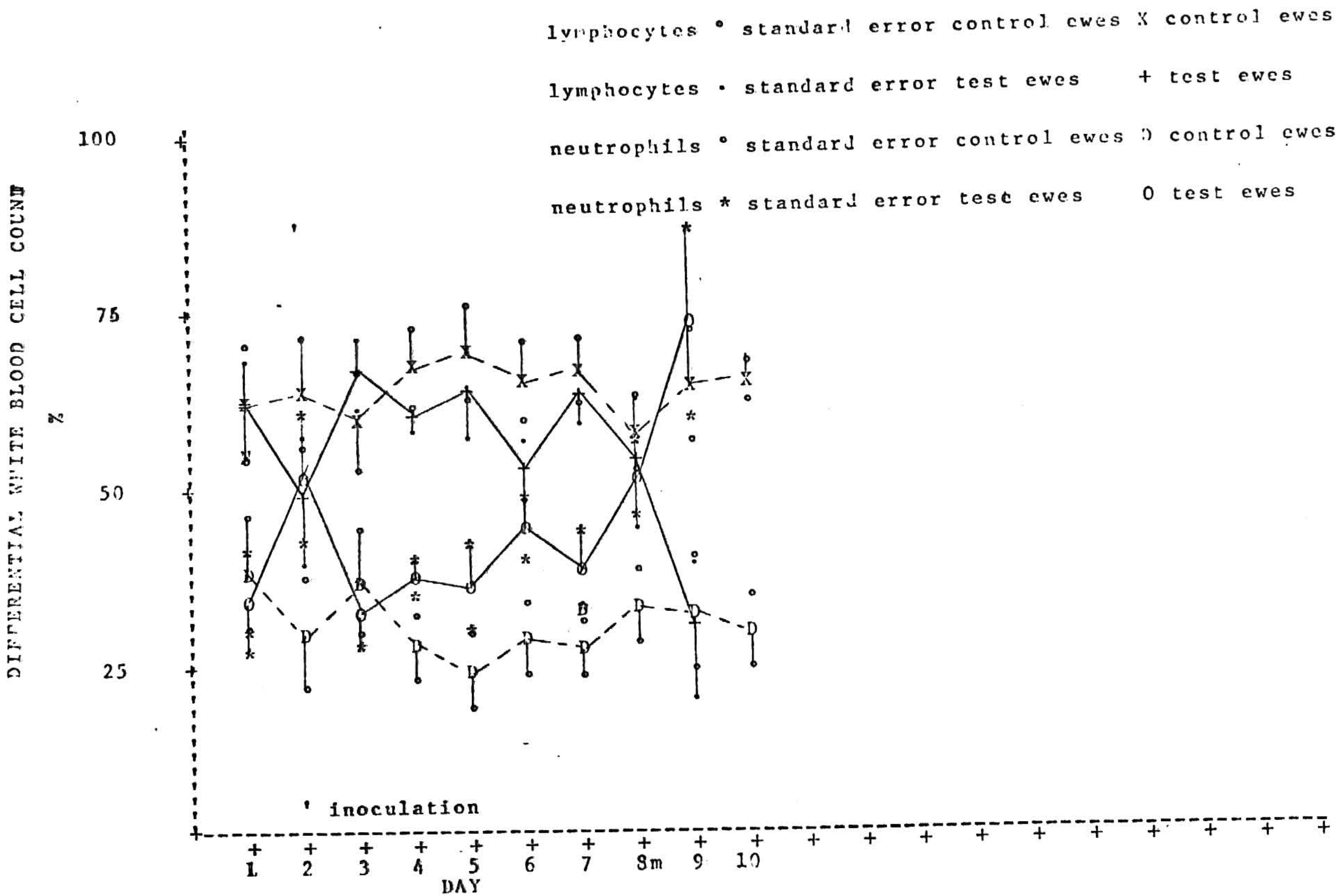


Figure 17. Differential white blood cell numbers for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

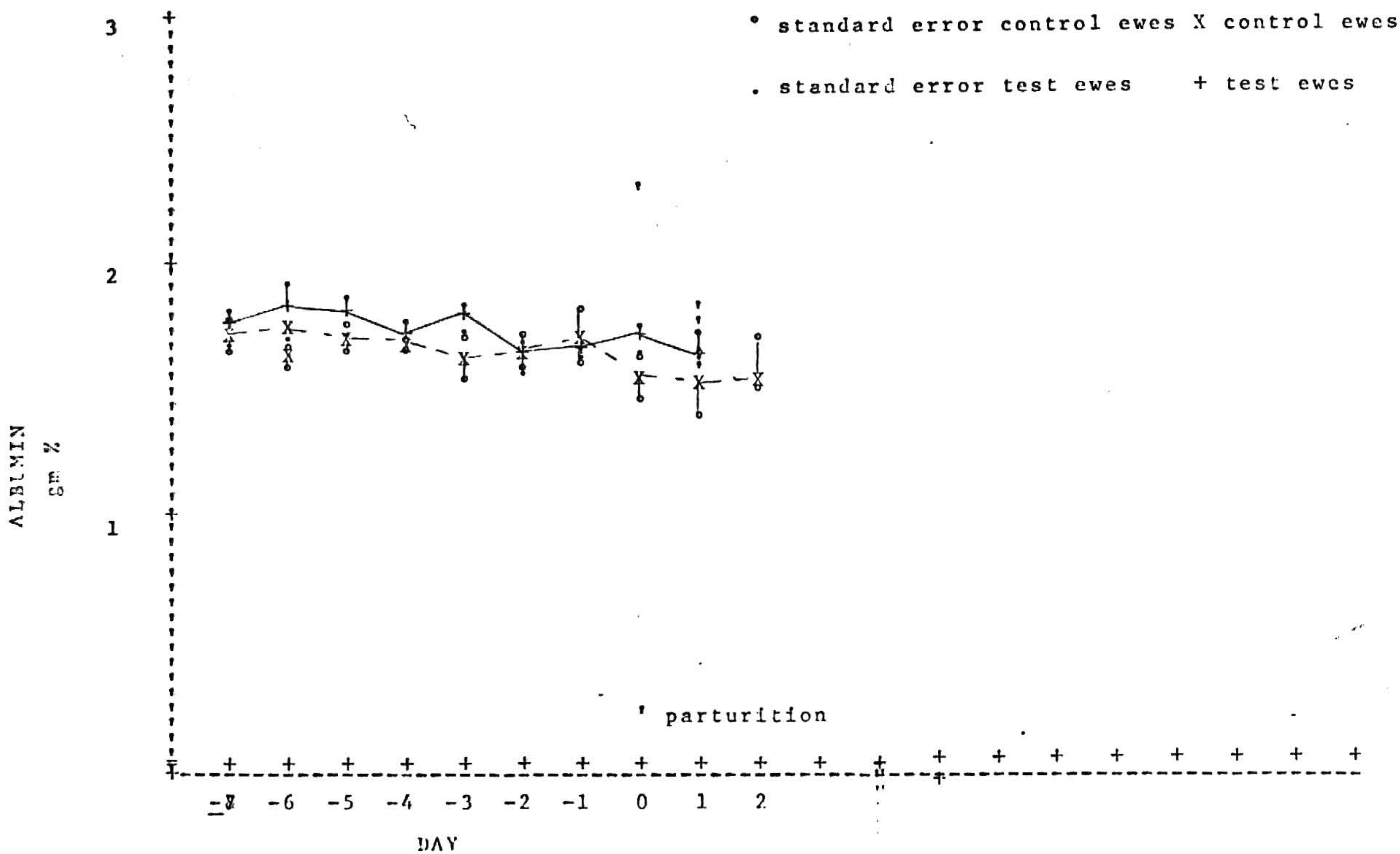


Figure 13. Serum albumin levels for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

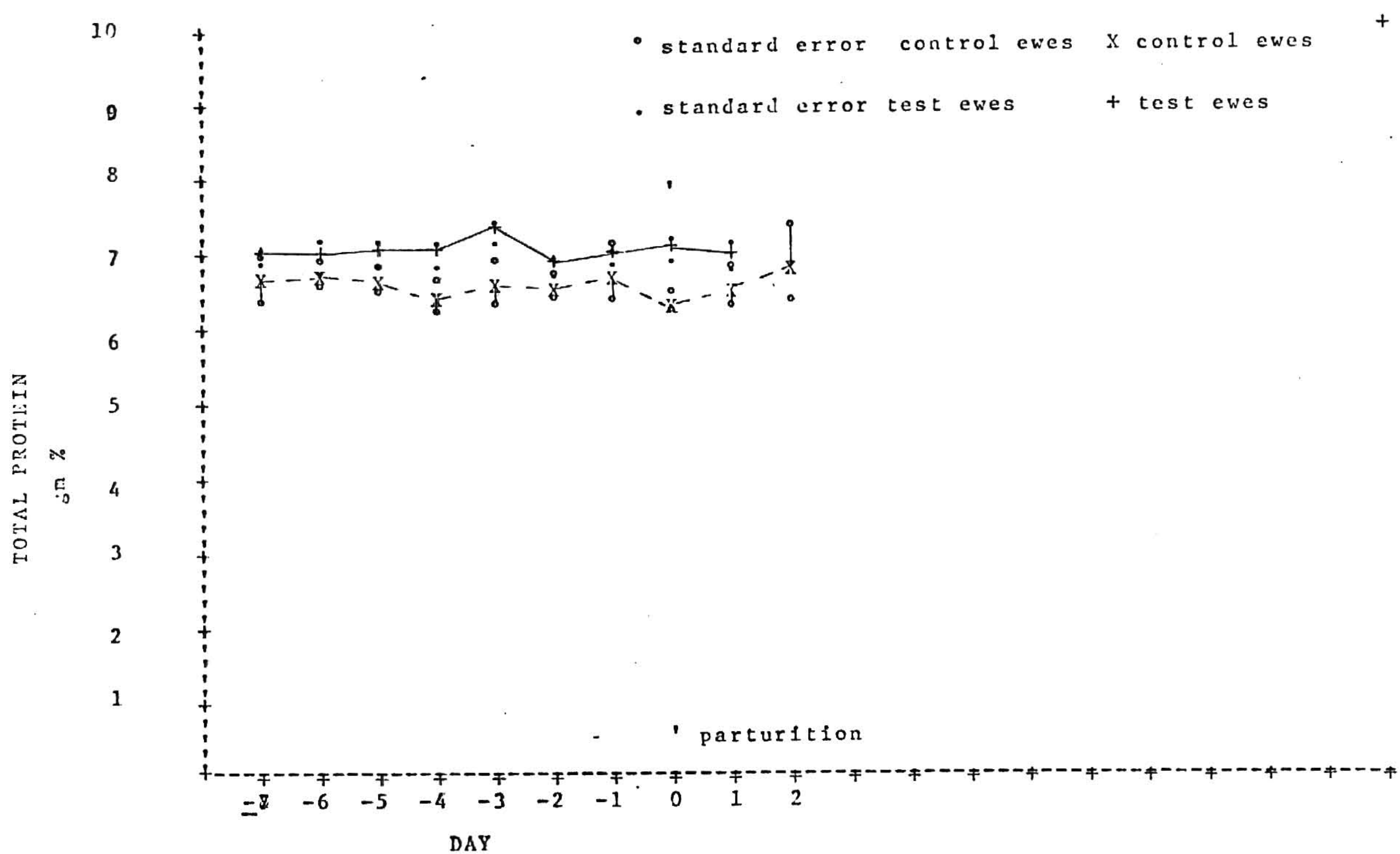


Figure 19. Serum total protein levels for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

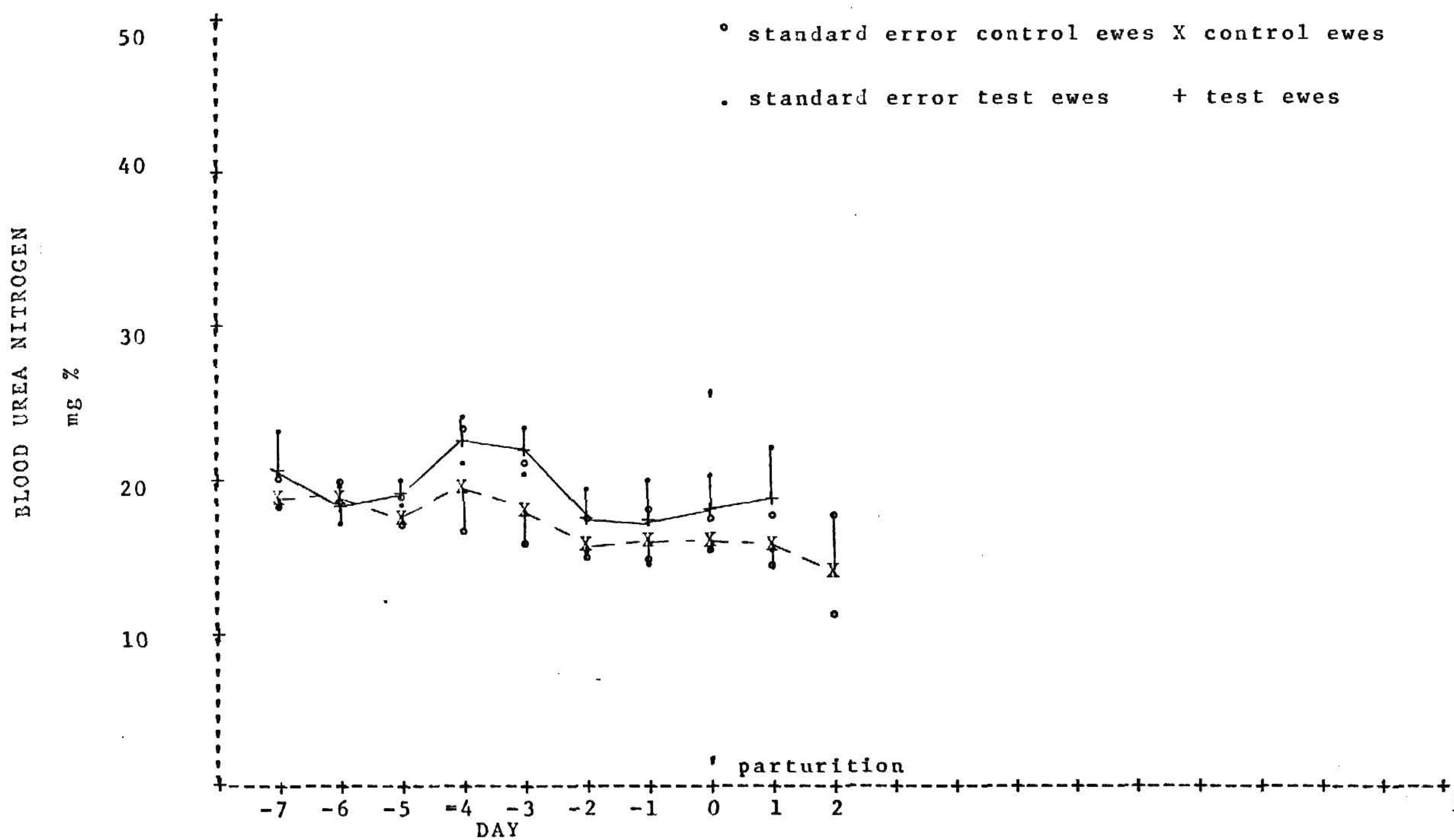


Figure 20. Serum BUN levels for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

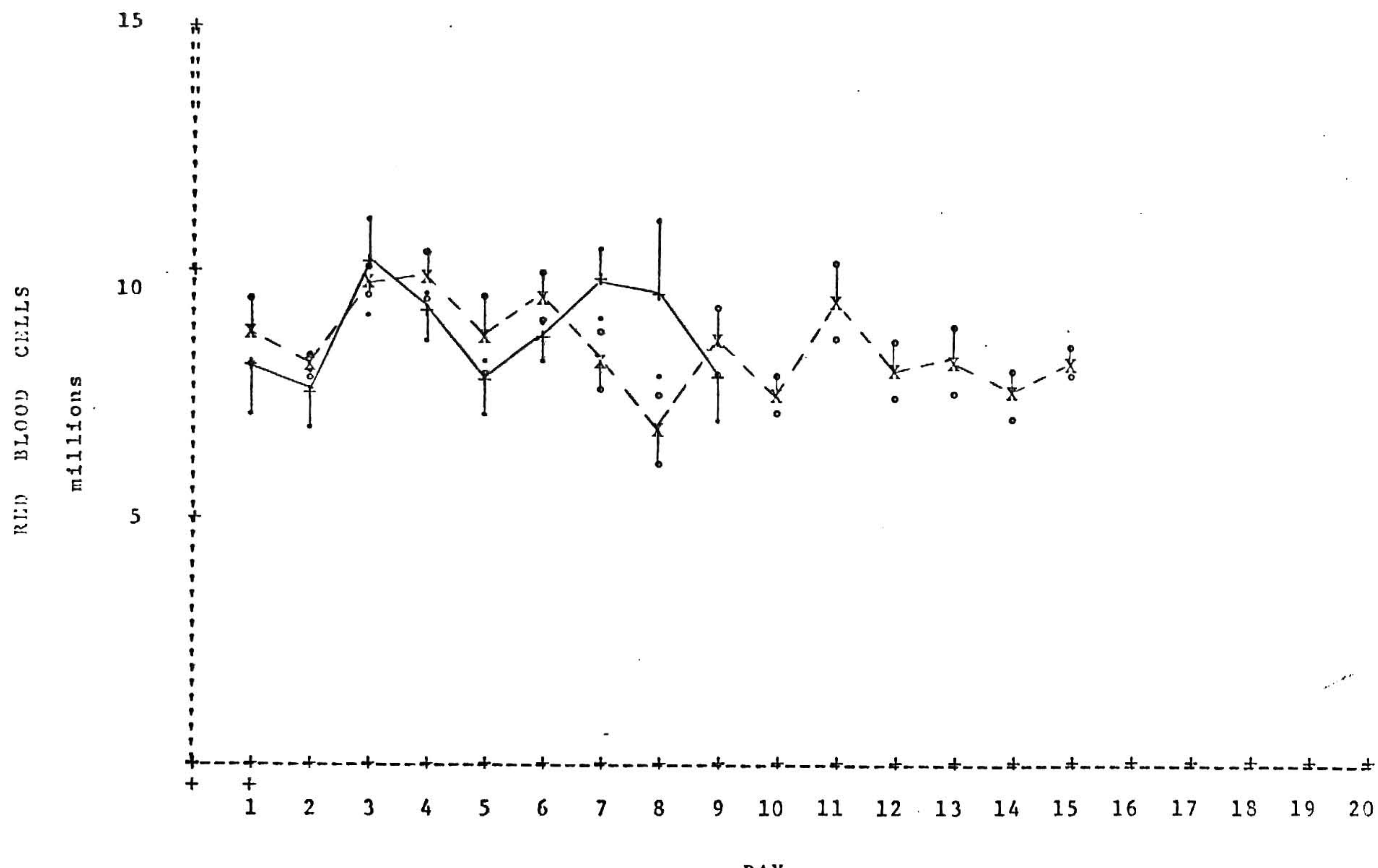


Figure 21. Red blood cell numbers for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

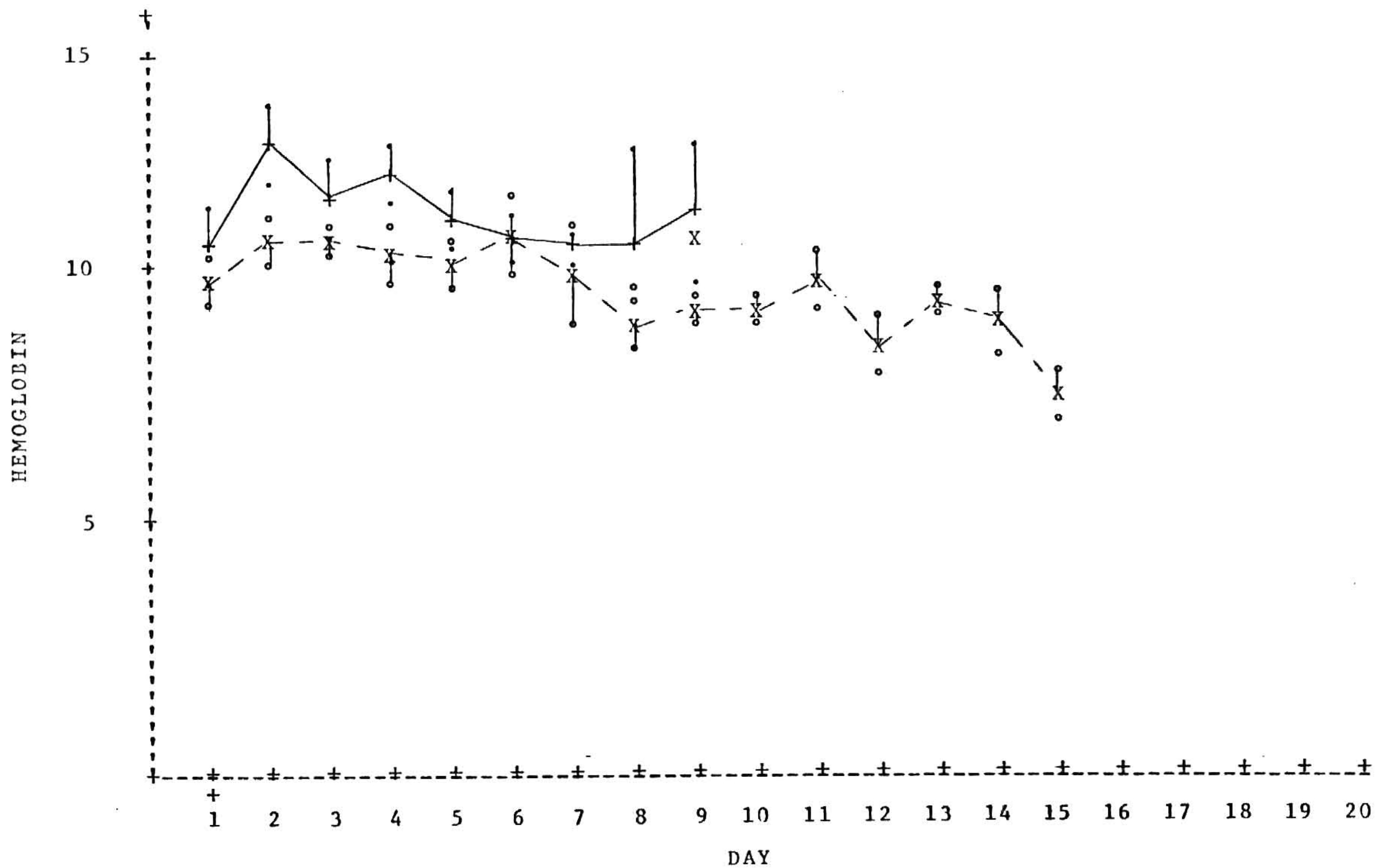


Figure 22 . Hemoglobin concentrations for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

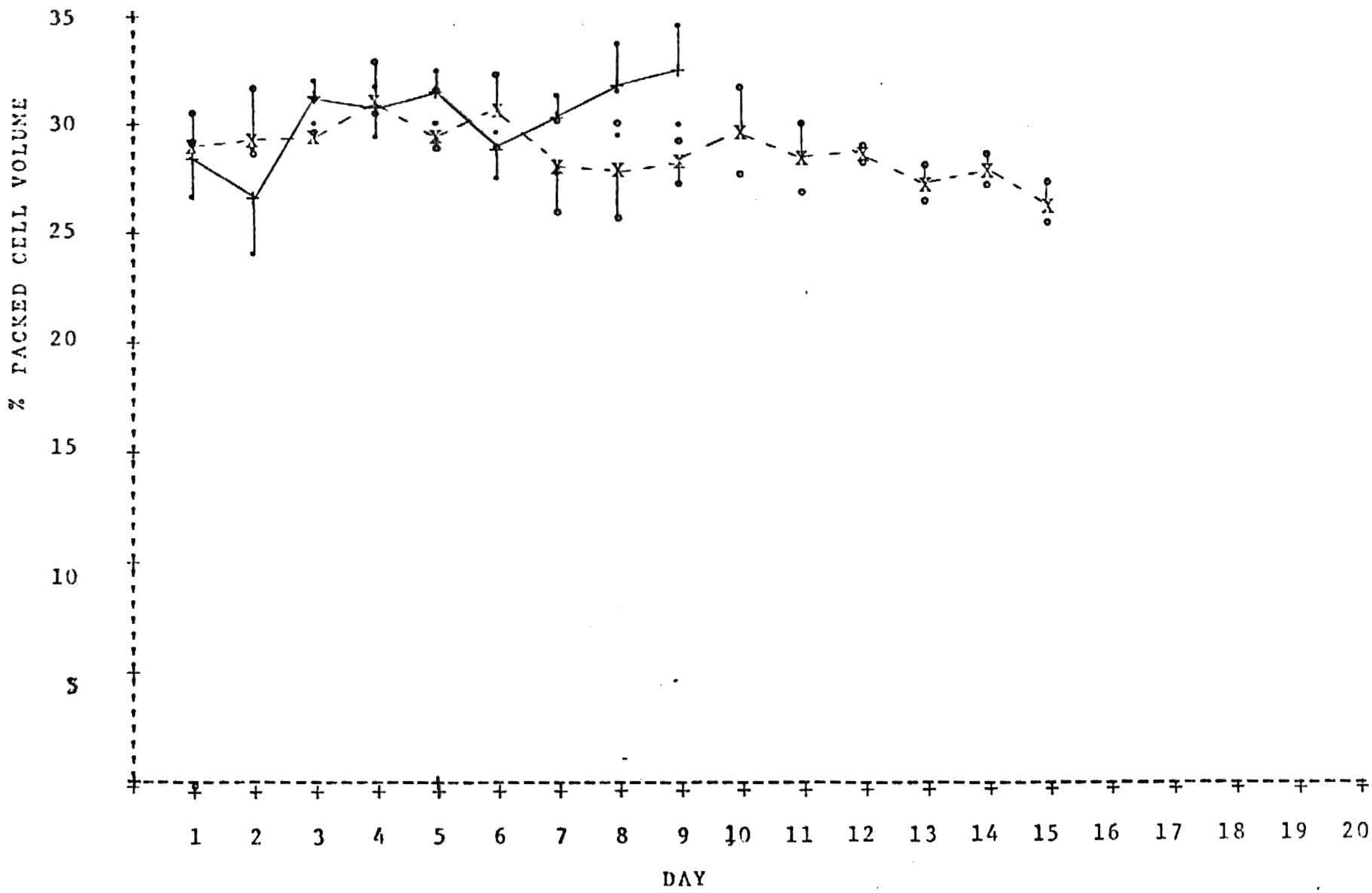


Figure 23. Packed cell volume for control pregnant ewes prior to and post-partum' test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard errpp of the means.

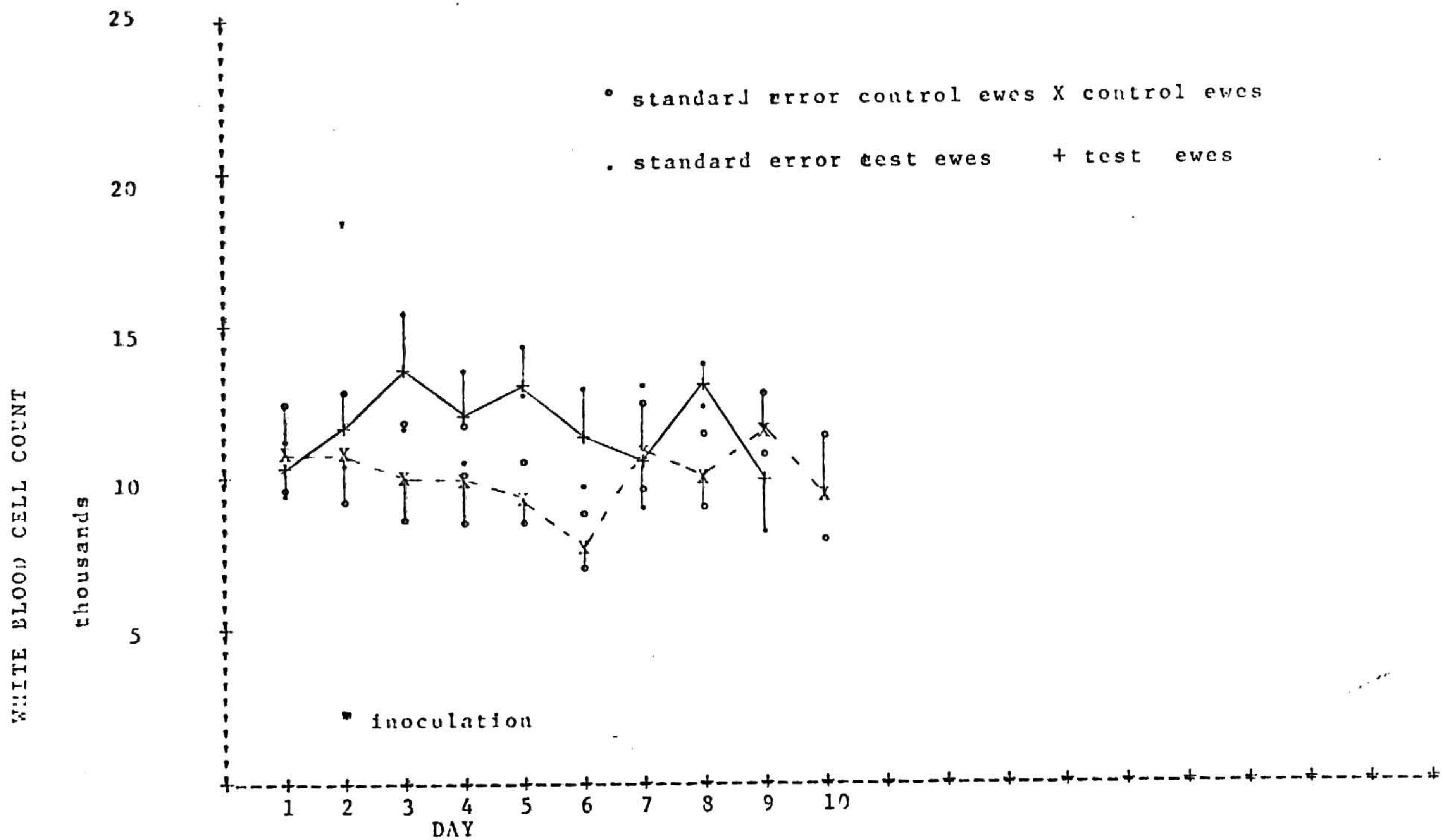


Figure 24. White blood cell numbers for control pregnant ewes prior to and post-partum test ewe data included for comparison, day 0 normalized for parturition. The vertical bars represent standard error of the means.

ACKNOWLEDGEMENTS

I would like to thank Dr. James Cook, Dr. Stan Dennis and Dr. David Chen for their help and guidance with this project. Dr. Dennis helped me organize the experiment. Dr. Chen taught me the methods required for radioimmunoassay, and Dr. Chen and Dr. Cook gave me good advice on writing of the thesis.

I also enjoyed working with Dr. Darrel Johnson in collecting the blood specimens from the ewes. Thanks are also due to my wife, Gloria, for her moral support and encouragement.

IV. APPENDIX

Progesterone Levels of Peripheral Serum of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 1

	Infected Ewes												Control Ewes			
Day	341	342	343	344	352	370	381	394	395	396	397	398	354	355	356	391
-39*															2.6	
-38															5.5	
-37															7.0	
-36															7.5	
-35															12.7	
-34															9.6	
-33															11.6	
-32															8.6	
-31															12.5	
-30															12.5	
-29														3.4	6.0	
-28														4.1	8.8	
-27														5.1	8.5	
-26														4.8	13.0	
-25														6.1	7.8	
-24														10.8	9.6	
-23														6.6	11.2	
-22														6.7	4.9	
-21														4.0	9.5	
-20													7.6	6.1	13.2	
-19													7.4	4.0	16.1	
-18													6.2	3.6	4.3	
-17													6.9	4.8	4.3	4.3
-16													6.5	5.0	13.3	5.0
-15													6.8	6.0	5.6	0.0
-14													8.6	3.8	1.6	0.0
-13													6.6	0.0	8.1	8.6
-12													7.4	2.1	2.7	12.2
-11													7.8	3.9	4.1	7.7
-10									5.9				6.0	3.0	8.0	8.1
- 9									5.3				5.9	6.9	7.6	8.1
- 8							14.8		6.6				6.4	5.2	10.5	14.2
- 7		5.7		7.0		13.0	9.3	4.8	6.2	5.1	14.8	2.1	11.5	11.8	6.1	6.9
- 6	2.9	5.9		10.1		6.9	11.7	6.5	8.9	2.8	9.2	2.2	8.0	8.0	9,5	7.0
- 5	5.3	9.0	4.8	8.5		11.9	15.1	10.9	5.6	0.8	13.8	0.0	7,7	5.5	5.5	4.6
- 4		7.0	6.8	6.1	5.2	14.6	10.3	12.7	11.8	6.4	17.1	21.3	8.0	5.0	6.8	4.8
- 3	5.3	5.9	7.2	8.6	5.2	11.4	13.2	11.2	11,6	0.0	22.2	19.4	7.9	2.1	4.7	2.9
- 2	5.5	8.6	6.6	9.1	5.9	12.7	11.8	7.1	9.1	5.5	7.4	7.3	5.4	23.1	3.8	2.9
- 1	5.5	11.6	4.3	8.8	4.6	12.1	5.5	17.4	5.5	15.7	7.2	0,0	500	4.2	.5	20.5
Delivery	2.7	2.9	4.7	7.1	2.4	2.5	1.3	0.0	.6	21.2	3.4	0.0	3.3	1.7	14.8	2.9
1		0.0	3.1		.2	.5	0.0	0.0	5.2		3.4		4.1	0.0	5.9	5.9
2													1.1			0.0

* - Days are days pre-partum ** Ng./ml.

Estradiol Levels of Peripheral Serum of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 2

	Infected Ewes												Control Ewes			
Day	341	370	342	381	343	394	344	352	395	396	397	398	354	355	356	391
-9*													23**	116	219	91
-8		173		52		136			192		227	192	27	175	218	83
-7		194	49	56		227	152			82	182	166	39	116		65
-6		154	45	65		149	204			150	180	155		168	142	69
-5	65	143	29	71		231	102		90	112	211	150	34	186	147	72
-4		212	40	91	29	248	30	64		138	224		78	175	154	110
-3	60	178	69	146	44	201	160	66	57	79	179	223	32	140		57
-2	67	158	34	289		223	123	67	66	114	173	279	38	151	306	89
-1	75	256	42	195	146	160	51	51		132	187	153	52	168	456	83
Delivery	89	224	103	179	162	315	59	66	69	339	144	541	260	471	625	
1		113	55	200	212	225		49	69	75			296			
2														99		

* - Days are days pre-partum **pg./ml/

Cortisol Levels of Peripheral Serum of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 3

	Infected Ewes												Control Ewes			
Day	341	342	343	344	352	370	381	394	395	396	397	398	354	355	356	391
-39*															35**	
-38															33	
-37															35	
-36															45	
-35															33	
-34															21	
-33															22	
-32															50	
-31															52	
-30															32	
-29														25	20	
-28														42	18	
-27														32	27	
-26														39	31	
-25														34	30	
-24														35	28	
-23														47	40	
-22														100	25	
-21														51	12	
-20													50	49	30	
-19													57	87	23	
-18													69	69	25	
-17														35	37	54
-16													88	22	56	56
-15													181	35	161	3 4
-14													34	23	24	40
-13													21	24	28	45
-12													33	35	46	34
-11														42	29	68
-10									6				42	53	27	72
- 9							41		18			38	36	30	16	
- 8							81		35	21	48	38	24	36	28	53
- 7		136		97		34	41	35	20	14	39	36	25	33	25	46
- 6	70	103		238		39	53	18	27	17	30	59	45	54	26	29
- 5	81	293	98	73	38	87	87	23	20	8	25	46	37	29	22	36
- 4		115	93	64	39	42	65	24	25	14	23	57	54	65	31	44
- 3	78	95	82	103	43	34	44	20	31	16	27	99	42	45	28	64
- 2	69	82	55	56	29	37	41	11	26	30	16	60	25	30	38	30
- 1	97	43	53	39	31	32	35	15	26	40	28	33	76	27	68	79
Delivery	99	47	71	33	12	36	46	23	14	37	38	29	153	22	51	60
1		67	63			39	41	10	19		25			26		
2													32	24		

*Days pre-partum. **Ng./ml.

Red Blood Cell Count of Peripheral Blood of Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes.

Table 4

	Infected Ewes							Control Ewes				
Day	341	342	343	344	352	370	381	353	354	355	356	391
1*	7.8*	10.5	6.7	4.2	10.6	7.3	9.5	8.3	8.2	7.3	10.6	10.6
2	7.6	4.8	5.7	8.0	8.6	9.4	8.3	7.7	7.6	8.8	8.4	8.8
3	11.6	9.4	8.3	10.6	15.0	10.5	6.2	10.7	10.3	9.4	9.2	10.3
4	10.5	10.6	10.6	7.4	7.6	9.6	8.4	10.7	10.4	11.1	8.4	10.0
5	9.2	9.5	6.9	8.7	7.6	6.6	6.2	10.6	9.7	9.6	8.4	6.2
6	7.7	8.6	7.8	10.6	8.6	9.5	8.5	11.2	9.2	10.4	9.0	8.7
7		9.1	9.6	12.6		8.8	9.2	9.2	9.0	9.3	8.2	6.2
8		12/0		8.3		12.4	5.6	8.4	7.9	7.8	6.4	4.5
9		8.6		9.1		8.4	5.5	10.5	8.7	10.3	7.2	7.2
10							7.8	7.2	6.6	9.1	7.3	8.2
11							7.9	9.8	9.8	9.7	11.9	6.8
12								9.6	9.6	9.6	6.4	8.0
13								9.5	9.5	7.8	7.3	6.8
14								9.4	7.8	10.3	7.8	6.6
15								8.7	6.2	7.6	8.3	8.0
16								8.0	7.6	9.2	9.1	8.0
17								8.1	8.4	9.5	5.6	8.0
18								9.6	7.6	8.4	5.5	6.0
19								6.4	6.5	7.1	6.5	7.0
20									8.0	9.5	8.0	6.2
21									9.2	9.6	7.8	
22									8.6	8.9	6.8	
23									5.8	6.4	5.2	
24										6.5	7.0	
25										7.2	6.6	
26										8.4	7.8	
27										6.0	5.6	
28										8.2	6.7	
29										7.6	6.7	
30										7.6	6.7	
31										8.6	6.6	
32										6.8	7.5	
33											7.6	
34											7.8	
35											6.0	
36											5.6	
37											6.9	
38											6.1	
39											7.8	
40											7.5	

* Day of inoculation. ** millions per mililiter.

Hemoglobin concentration of Peripheral Blood of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

table 5

	Infected Ewes							Control Ewes				
Day	341	342	343	344	352	370	381	353	354	355	356	391
1*	8.8*	10.0	9.6	13.9	12.6	7.6	11.0	915	9.7	8.8	9.9	11.0
2	14.4	13.1	13.3	15.2	10.4	11.3	9.9	10.4	11.6	12.0	9.9	9.3
3	11.6	15.2	8.6	11.9	11.0	12.3	9.5	10.9	10.7	11.7	10.4	10.0
4	11.6	12.1	11.7	11.4	10.3	15.1	10.8	9.9	11.5	11.9	9.9	8.8
5	13.2	13.0	11.2	9.6	9.9	10.3	15.1	10.4	10.8	11.6	9.5	8.8
6	10/9	9.6	8.5	13.0	11.2	10.8	10.2	10.0	10.8	13.9	9.6	9.6
7	10.1	11.9	10.5	11.1	9.7	9.3	10.5	8.2	10.8	13.2	10.3	7.6
8		10.7		15.7		6.5	8.8	10.0	9.4	9.5	9.1	7.2
9		11.6				13.4	8.4	8.2	9.8	13.1	9.2	9.0
10							9.7	8.6	9.3	10.3	8.6	9.7
11							10.1	9.3	11.2	11.7	9.0	8.5
12								6.4	8.8	10.3	8.6	9.7
13								9.0	9.2	10.5	9.4	9.3
14								8.0	7.8	11.1	10.0	8.4
15								6.0	7.1	8.6	8.1	8.1
16								7.8	10.5	10.9	8.8	8.3
17								10.5	11.0	12.0	7.9	7.2
18								9.8	9.9	10.6	8.2	7.2
19									9.6	11.9	9.4	8.2
20									8.7	9.7	9.4	8.4
21									9.4	9.5	8.7	
22									9.6	10.3	9.1	
23										9.7	9.1	
24										9.4	9.5	
25										9.0	9.2	
26										10.1	9.4	
27										11.1	10.1	
28										9.7	9.4	
29										11.3	9.5	
30										11.4	9.6	
31										8.8	9.3	
32											8.1	
33											8.6	
34											9.2	
35											7.9	
36											8.5	
37											8.8	
38											9.0	
39											12.3	

* Day of Inoculation **

White Blood Cell Count of Peripheral Blood of Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes.

Table 6

	Infected Ewes							Control Ewes				
Day	341	342	343	344	352	370	381	353	354	355	356	391
1*	9.8*	12.7	12.5	6.5	9.6	8,4	12.8	14.9	8.4	12.3	7.0	11.4
2	7.4	15.5	10.4	16.9	11.0	9.1	11.0	11.1	17.4	9.1	9.0	7.2
3	16.8	21.3	16.8	8.9	13.6	11.9	9.5	7.4	15.6	8.3	11.4	7.6
4	13.0	19.0	9.7	13.8	11.9	9.5	7.0	15.9	9.0	10.0	7.0	7.8
5	13.3	15.9	14.7	16.3	14.1	9.7	7.0	12.4	7.5	10.2	9.7	6.8
6	17.0	10.0	13.7	16.0	9.0	7.0	6.5	11.1	7.0	6.7	6.0	7,7
7		15.9	11.2	7.8		8.2	9.3	10.5	7.3	15.5	11.7	8.9
8		14.6		13.1		13.4	11.0	7.1	11.7	12.7	11.3	7.0
9		9.7				7.0	12.9	13.7	12.9	13.1	9.3	8.7
10							10.2	7.9	9.2	15.8	6.7	7.2
11							10.8	7.0	12.5	14.0	7.4	8.0
12								7.3	7.1	10.4	8.1	7.0
13								12.9	11.5	12.5	7.0	11.6
14								7.0	12.0	11.2	14.3	11.5
15								6.5	13.5	6.5	9.5	11.5
16								6.5	11.0	12.5	6.5	9.6
17								8.6	12.3	11.8	11.6	11.2
18								9.0	9.1	14.3	9.1	12.0
19								7.1	8.3	9.8	10.9	8.9
20								11.2	13.4	9.0		9.2
21									8.5	9.4	7.0	
22									7.9	11.0	9.3	
23									11.0	11.9	6.8	
24										11.9	6.8	
25										7.3	7.1	
26										12.6	12.6	
27										10.0	9.2	
28										10.9	10.3	
29										9.1	8.6	
30										11.8	7.7	
31										10.3	10.7	
32										11.6	11.5	
33											10.7	
34											10.4	
35											11.7	
36											7.5	
37											7.0	
38											12/7	
39											9.4	
40											11.2	

* Day of Inoculation. ** Thousands per ml.

Packed Cell Volume of Peripheral Blood of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 7

	Infected Ewes							Control Ewes				
Day	341	342	343	344	352	370	381	353	354	355	356	391
1*	31**	30	26	23	28	33	28	31	31	26	31	29
2	31	16	21	26	31	35	28	31	32	33	28	25
3	32	31	31	35	30	34	27	29	30	33	30	28
4	34	35	27	29	29	34	29	31	34	36	30	28
5	36	32	32	31	29	35	27	30	33	33	27	27
6	34	30	27	30	30	27	25	30	33	35	29	25
7	36	32	29	30		27	29	31	31		27	22
8		32		35		35	26	27	31	33	27	20
9		32				37	29	27	29	31	28	25
10							26	31	29	36	26	25
11							29	30	30	32	25	24
12								28	29	29	292	27
13								26	27	30	26	26
14								27	28	30	27	26
15								25	25	29	27	24
16								26	26	30	25	26
17								25	29	299	25	27
18								28	28	29	24	29
19								25	29	28	24	27
20									26	30	26	29
21									29	29	28	
22									28	28	27	
23								28	28	28	27	
24										27	27	
25										28	26	
26										27	26	
27										28	25	
28										30	27	
29										30	26	
30										30	25	
31										30	29	
32										29	24	
33											26	
34											27	
35											28	
36											26	
37											26	
38											27'	
39											29	
40											31	

* Day of Inoculation. ** Percentage of whole blood formed by red blood cells.

Percentage Neutrophils in Peripheral Blood of Pregnant Ewes Infected with *Listeria monocytogenes* and in Normal Control Ewes.

Table 8

Day	Infected Ewes							Control Ewes				
	341	342	342	344	352	370	381	353	354	355	356	391
1*	73	20	23	26	33	39	20	68	36	24	25	35
2	63		26	54	72	21	69		12	38	20	39
3	47	46	19	33	14	32	29	52	52	38	17	22
4	36	34	50	32	28	36	50	27	30	45	18	12
5	42	33	25	25	64	15	43		18	46	12	29
6	42	50	27	45	38	31	57	14	24	43	24	35
7	29	27	25	37		56	52	32	18	34		22
8		38		53		48	63	24	40	34	18	46
9		59					80	24	58	38	26	11
10							73	17	44	25	21	37
11								27	30	36	20	42
12								27	30	33	25	43
13								29	27	33	31	71
14								28	27	33	46	54
15								15	43	45	19	54
16								27	24	44	14	55
17								18	29	42	28	43
18								28	18	39	72	
19								34	52	34	31	
20									41	45	23	
21									40		40	
22									33	36	20	
23										27	19	
24										54	21	
25										40	24	
26										38	44	
27										43	19	
28										59	21	
29										44	35	
30										46		
31												
32											39	
33											54	
34											32	
35											26	
36											55	
37											59	
38											56	

* Day of inoculation.

Jugular Levels Of SGOT* in Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 9

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	391
-39**										123	
-38										125	
-37										116	
-36										117	
-35								107		107	
-34										105	
-33										101	
-32										88	
-31										88	
-30										84	
-29									127	75	
-28									128	95	
-27									114	97	
-26									114	84	
-25									107	86	
-24									100	80	
-23									98	76	
-22									91	75	
-21									130	72	
-20								117	155	75	
-19								121	185	73	
-18								121	200	75	
-17								123	185	77	73
-16								115	150	80	86'
-15								113	117	90	80
-14								108	108	97	74
-13								104	121	87	70
-12								85	110	98	66
-11								81	111		69
-10								97	114	75	69
- 9							90	85	109		70
- 8							116	90	80	67	64
- 7		97		107		165	112	81	92	75	
- 6	82	105		114		160	94	75	122	80	72
- 5	96	107	90	96		180	95	80	122	78	
- 4	104	115	94	97	85	182	95	75	90	80	84
- 3	130	124	113	101	89	182	102	84	86	69	66
- 2	125	90	99	105	90	148	96	70	92 7	78	70
- 1	129	137	92	80	86	250	99	80	110	80	84
Day of Delivery	135	152	130	99	79	197	100	95	110	80	62
1 Day Post-Partum		127	98		94	160	112	100	114		70
2 Days Post-Partum									105		75

* SGOT concentrations in K. Units. **- days are days pre-partum.

Jugular Levels of Alkaline Phosphatase* in Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes.

Table 10

Day	Infected Ewes							Control Ewes			
	341	342	343	344	352	370	381	354	355	356	381
-39**										13.0	
-38										10.6	
-37										11.0	
-36										11.3	
-35										10.1	
-34										11.2	
-33										8.9	
-32										8.0	
-31										11.4	
-30										10.8	
-29									16.2	7.0	
-28									13.0	13.0	
-27									14.0	10.0	
-26									12.2	8.0	
-25									14.0	8.0	
-24									12.1	10.8	
-23									11.0	9.0	
-22									10.8	10.5	
-21									10.1	12.5	
-20								17.0	10.0	10.0	
-19								24.0	14.0	9.1	
-18								20.5	14.2	14.2	
-17								18.0	13.0	12.8	
-16								15.5	9.0	13.0	
-15								15.5	8.0	12.3	10.0
-14								17.0	9.5	10.0	11.1
-13								14.0	10.5	13.8	10.0
-12								13.0	12.0	13.5	11.0
-11								14.0	10.5	13.8	10.0
-10								13.0	12.0	13.5	14.3
- 9							8.5	18.0	13.0	15.3	12.6
- 8							6.5	27.0	15.5	15.0	11.2
- 7		15.2		17.6		10.9	8.5	17.0	12.5	16.0	9.0
- 6	17.7	14.8		18.0		10.0	7.8	20.0	12.2	15.0	13.0
- 5	18.8	13.9	12.2	21.1		8.0	8.0	27.0	15.5	15.0	11.0
- 4	14.3	15.6	8.0	16.2	28.0	10.0	7.0	17.0	13.3	12.0	11.5
- 3	15.0	14.5	8.5	18.9	23.0	10.0	8.0	16.0	9.0	12.0	11.0
- 2	10.0	9.0	8.3	14.9	17.0	9.0	7.5	19.0	10.1	15.0	10.0
- 1	10.0	14.0	7.0	12.0	15.0	9.0	7.0	14.9	10.0	15.0	12.0
Day of Delivery	9.8	15.0	14.0	15.0	19.0	10.8	8.2	16.1	10.0		7.5
1 Day Post-Partum		25.0	8.0	b	17.0	7.0	8.5	16.1	10.0		7.5
2 Days Post-Partum									13.8		9.8

* Alkaline Phosphatase concentrations in K. A. Units. ** - days are days pre-partum.

Jugular Levels of Lactic Dehydrogenase* in Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes.

Table 11

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	381
-39**										179	
-38										165	
-37										163	
-36										160	
-35										155	
-34										155	
-33										160	
-32										142	
-31										152	
-30										145	
-29									225	92	
-28									207	145	
-27									193	135	
-26									190	119	
-25									194	120	
-24									185	132	
-23								188	188	100	
-22									180	137	
-21									180	156	
-20								210	199	130	
-19								200	240	125	
-18								175	200	144	
-17								175	240	130	146
-16								169	225	140	153
-15								173	210	133	146
-14								165	158	220	138
-13								158	220	132	174
-12								143	209	175	122
-11								170	224	140	117
-10								170	210	115	131
- 9							185	150	220	148	142
- 8							147	151	132	115	114
- 7		204		224		296	155	145	205	130	115
- 6	184	204		205		222	170	139	230	155	109
- 5	230	182	157	168		232	174	139	227	160	101
- 4	166	175	150	165	214	250	110	130	195	155	150
- 3	168	173	127	174	193	186	166	v99	199	85	114
- 2	160	110	126	165	174	230	157	131	195	159	125
- 1	180	206	114	145	175	300	146	150	239	155	160
Day of Delivery	173	179	179	165	171	279	181	160	226	165	71
1 day post-partum		182	120		205	219	155	157	218		80
2 Days post-partum									235		83

* LDH concentrations in W. units. ** - days are days pre-partum.

Jugular Levels of Glucose* of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 12

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	381
-39**										66	
-38										56	
-37										50	
-36										46	
-35										50	
-34										50	
-33										49	
-32										64	
-31										60	
-30										55	
-29									79	56	
-28									60	62	
-27									52	59	
-26									50	46	
-25									55	46	
-24									50	55	
-23									57	55	
-22									50	54	
-21									71	64	
-20								95	60	49	
-19								64	56	40	
-18								46	60	45	
-17								46	60	55	55
-16								50	40	42	51
-15								44	50	50	36
-14								45	60	73	45
-13								44	65	44	67
-12								55	60	77	58
-11								45	67	64	64
-10								46	52	60	47
- 9							53	51	43	64	45
- 8							53	60	46	60	60
- 7		75		52		78	45	35	55	63	61
- 6	118	55		81		85	66	45	45	64	64
- 5	60	55	72	66		40	55	69	50	86	65
- 4	67	46	54	65	52	50	50	55	59	91	50
- 3	62	42	59	55	55	55	30	56	46	60	75
-n2	57	65	76	56	49	60	37	60	66	85	74
- 1	87	52	57	80	60	70	47	44	65	65	95
Day of Delivery	72	65	44	70	67	70	69	35	85	90	75
1 Day Post-Partum		115	93	53	40	45		45	180	70	
2 Days Post-Partum								25	190		92

* Glucose concentrations in mg. %. ** - days are days pre-partum.

Jugular Levels of Blood Urea Nitrogen* of Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes.

Table 13

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	381
-37**										33	
-36										25	
-35										22	
-34										17	
-33										17	
-32										17	
-31										17	
-30										14	
-29									33	14	
-28									25	16	
-27									21	20	
-26									17	19	
-25								8	19	20	
-24									18	19	
-23									17	17	
-22									16	22	
-21									12	14	
-20								27	19	22	
-19								10	18	17	
-18								17	15	19	
-17								14	20	17	15
-16								14	22	22	27
-15								13	22	22	24
-14								14	19	17	16
-13								12	17	22	13
-12								9	18	17	15
-11								12	18	22	21
-10								19	24	21	21
- 9							16	12	18	22	21
- 8							19	16	21	21	17
- 7		19		21		15	27	16	19	20	20
- 6	15	21		21		17	17	17	20	20	18
- 5	20	20	16	21		20	17	15	19	17	19
- 4	23	18	21	23	27	28	17	12	24	16	26
- 3	24	19	23	20	23	28	15	13	24	21	14
- 2	27	16	17	16	21	10	14	13	19	17	14
- 1	29	12	22	12	22	19	14	15	19	16	14
Day of Delivery	29	11	14	16	22	19	14	15	19	16	14
1 Day Post-Partum		12	12		26	16	27	8	19		14
2 Days Post-Partum									19		15

* Blood Urea Nitrogen concentrations in mg. %. ** - days are days pre-partum.

Jugular Levels of Uric Acid* of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 14

Day	Infected Ewes							Control Ewes			
	341	342	343	344	352	370	381	354	355	356	381
-39**										.40	
-38										.39	
-37										.30	
-36										.26	
-35										.00	
-34										.20	
-33										.19	
-32										.17	
-31										.25	
-30										.30	
-29									.30	.20	
-28									.30	.31	
-27									.30	.45	
-26									.12	.20	
-25									.20	.20	
-24									.08	.50	
-23									.20	.30	
-22									.19	.39	
-21									.10	.32	
-20								.40	.20	.50	
-19								.30	.40	.49	
-18								.30	.34	.51	
-17								.09	.24	.25	.40
-16								.21	.20	.70	.50
-15								.11	.18	.60	.25
-14								.21	.22	.60	.29
-13								.29	.30	.70	.39
-12								.10	.23	.60	.51
-11								.11	.40	.50	.42
-10								.11	.40	.40	.50
- 9							.50	.49	.22	.59	.51
- 8				.20			.44	.48	.39	.62	.48
- 7		.02		.17		.28	.58	.12	.23	.35	.40
- 6	.10	.00		.10		.30	.69	.10	.60	.55	.32
- 5	.10	.00	.21	.11		.20	.52	.60	.51	.62	.70
- 4	.02	.00	.19	.18	.50	.35	.30	.20	.61	.52	.50
- 3	.08	.05	.18	.18	.18	.20	.50	.30	.41	.30	.50
- 2	.10	.00	.30	.18	.21	.20	.50	.30	.40	.62	.51
- 1	.20	.00	.19	.30	.12	.29	.80	.40	.50	.54	.60
Day of Delivery	.18	.10	.11	.19	.27	.30	.90	.40	.20	.60	.30
1 Day Post-Partum		.21	.19		.31	.20	.58	.30	.50	.30	.30
2 Days Post-Partum									.68		.30

* Uric Acid concentrations in mg. %. ** - days are days pre-partum.

Jugular Levels of Total Protein* of Pregnant Ewes Infected with'

Listeria monocytogenes and in Normal Control Ewes.

Table 15

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	381
-39**										7.2	
-38										7.4	
-37										7.6	
-36										7.3	
-35										7.3	
-34										7.5	
-33										7.4	
-32										7.2	
-31										7.2	
-30										7.1	
029									7.1	7.0	
-28									7.3	7.0	
-27									7.4	6.9	
-26									7.2	7.1	
-25									7.5	7.0	
-24									7.2	6.6	
-23									7.2	6.6	
-22									7.1	6.6	
-21									6.9	6.4	
020								8.0	7.0	6.6	
-19								7.9	6.8	6.3	
-18								7.8	6.8	6.2	
-17								8.1	6.6	6.4	7.1
-16								7.8	6.7	6.3	7.1
-15								7.9	6.5	6.0	7.0
-14								8.2	6.5	7.0	6.9
-13								7.7	6.7	6.0	7.0
-12								8.0	6.5	7.0	6.7
-11								7.8	6.3	6.2	6.8
-10								8.6	6.6	6.1	7.0
- 9							6.6	7.4	6.5	6.2	7.1
- 8							6.9	7.4	6.5	6.5	6.4
- 7		7.1		7.1		7.0	6.7	7.5	6.3	6.1	6.6
- 6	6.5	7.1		7.7		7.1	6.4	7.1	6.8	6.3	6.5
- 5	6.9	7.4	6.9	6.9		7.5	6.4	6.9	6.2	6.4	6.9
- 4	7.3	7.4	6.8	7.0	6.4	7.5	6.5	7.0	6.3	6.0	6.2
- 3	7.1	7.2	7.9	7.1	7.0	7.9	6.9	7.2	6.5	5.8	6.7
- 2	6.9	7.0	7.2	6.9	7.1	6.1	6.7	6.6	6.1	6.4	6.9
- 1	7.1	7.3	7.3	6.7	7.0	6.8	6.6	7.2	5.8	6.3	7.4
Day of Delivery	7.0	7.3	7.2	7.1	6.7	7.0	6.4	6.3	6.3	6.0	6.6
1 Day Post-Partum		7.5	7.3		6.8	6.5	6.7	6.6	6.0		6.9
2 Days Post-Partum									6.3		7.3

*Total Protein concentrations in gm. %. ** - days are days pre-partum.

Jugular Levels of Calcium* of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 16

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	381
-37**										9.0	
-36										9.8	
-35										10.3	
-34										9.9	
-33										9.6	
-32										9.8	
-31										9.8	
-30										9.8	
-29										9.9	
-28										9.7	
									9.2	9.8	
-27									9.4	10.5	
-26									10.3	10.5	
-25									9.7	9.8	
-24									10.0	9.5	
-23									9.5	9.1	
-22									10.0	9.8	
-21									9.6	10.3	
-20								8.3	9.8	10.6	
-19								9.4	9.8	10.0	
-18								8.5	9.8	9.5	
-17								9.4	9.6	9.9	
-16								9.3	9.8	9.6	8.4
-15								8.9	9.3	9.6	8.4
-14								9.0	9.0	9.6	8.7
-13								8.3	9.8	9.2	9.0
-12								8.9	10.0	9.2	9.3
-11								9.0	9.8	9.6	9.1
-10								9.4	10.2	9.5	9.1
- 9							9.9	9.0	9.7	10.5	9.4
- 8							9.5	9.2	9.6	8.5	8.9
- 7		9.5		9.3		10.0	9.6	9.0	9.8	9.6	9.0
- 6	9.4	9.1		10.3		10.2	8.9	8.8	9.4	9.7	8.5
- 5	9.9	9.3	10.4	9.4		8.4	8.7	8.6	9.5	9.7	8.9
- 4	9.4	9.3	9.0	9.1	9.8	8.2	8.4	9.0	9.4	9.4	9.3
- 3	8.8	9.3	10.5	9.4	9.1	9.3	8.7	9.4	9.2	9.2	8.5
- 2	8.6	9.8	10.0	9.3	9.3	6.3	8.6	8.5	8.9	9.7	8.6
- 1	8.5	9.4	10.1	9.2	9.3	8.3	9.1	9.0	9.0	9.8	9.4
Day of Delivery	8.6	9.8	9.2	9.5	9.3	9.5	9.0	8.4	9.2	9.4	8.6
1 Day Post-Partum		10.3	10.0		8.9	6.6	9.6	8.9	9.0		6.1
2 Days Post-Partum									9.5		9.7

*Calcium concentrations in mg. %. ** - days are days pre-partum.

Jugular Levels of Phosphorous* of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 17

Day	Infected Ewes							Control Ewes			
	341	342	343	344	352	370	381	354	355	356	381
-39**										4.6	
-38										3.2	
-37										4.0	
-36										5.2	
-35										5.6	
-34										6.2	
-33										5.6	
-32										6.2	
-31										5.6	
-30										5.5	
-29										4.3	
-28										4.6	
-27									4.0	5.0	
-26									3.0	4.6	
-25									4.4	5.1	
-24									4.3	5.1	
-23									4.8	4.8	
-22									3.7	4.2	
-21									4.3	3.9	
-20								7.9	4.8	4.9	
-19								7.0	4.3	4.4	
-18								6.5	3.9	5.0	
-17								7.6	4.8	3.7	4.3
-16								8.7	4.5	4.5	6.9
-15								8.3	4.6	4.0	5.2
-14								8.2	3.9	4.9	5.5
-13								7.8	4.3	5.1	4.6
-12								6.4	4.1	5.4	6.3
-11								4.8	4.1	4.8	5.9
-10								3.5	4.1	5.4	5.6
- 9							5.2	5.5	5.1	3.9	5.5
- 8							4.2	8.4	3.8	4.2	4.8
- 7		2.7		4.5		5.1	6.1	6.7	4.5	4.3	4.1
- 6		3.8		5.0		5.4	9.3	7.4	4.4	4.6	4.5
- 5	5.5	4.3	5.1	6.3		6.1	8.9	6.7	4.8	3.9	4.0
- 4	5.6	4.1	4.0	5.1	5.8	7.0	7.9	4.5	4.6	4.4	3.6
- 3	4.9	5.6	5.5	5.5	4.4	5.8	7.5	5.3	4.2	3.9	4.7
- 2	4.7	5.8	5.2	4.7	5.4	4.0	6.3	5.5	3.1	3.1	4.3
- 1	4.8	5.2	5.0	3.7	4.5	5.3	7.3	5.1	2.6	5.0	4.8
Day of Delivery	4.6	5.4	5.8	4.0	5.3	4.4	6.3	5.5	3.3	3.9	4.8
1 Day Post-Partum		6.5	4.7		6.0	4.6	6.1	7.0	4.2		3.8
2 days Post-Partum								3.5	4.3		5.0

*Phosphorous concentrations in mg. %. ** - days are days pre-partum.

Jugular Levels of Albumin of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 18

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	381
-39**										3.4	
-38										3.4	
-37										3.5	
-36										1.8	
-35										1.8	
-34										2.0	
-33										1.8	
-32										1.8	
-31										2.0	
-30										1.9	
-29										1.8	
-28									.5	1.9	
-27									3.1	1.8	
-26									3.4	1.8	
-25									1.7	1.8	
-24									118	1.7	
-23									1.7	1.7	
-22									2.0	1.7	
-21									1.7	1.8	
-20								2.1	1.7	1.7	
-19								.4	1.7	1.8	
-18								2.0	1.8	1.7	1.6
-17								1.9	1.6	1.7	1.7
-16								2.0	1.6	1.7	1.6
-15								2.2	1.6	1.8	1.6
-14								2.0	1.7	1.8	1.6
-13								1.9	1.8	1.9	1.6
-12								1.9	1.7	1.7	1.7
-11								1.9	1.7	1.7	1.7
-10							1.8	1.6	1.7	1.7	1.7
- 9							1.9	2.0	1.7	1.7	1.8
- 8							1.9	2.0	1.7	1.5	1.6
- 7		1.7		2.0		1.7	1.8	1.9	1.7	1.7	1.7
- 6	1.8	1.7		2.3		1.8	1.7	1.8	1.7	1.7	1.6
- 5	2.1	1.7	1.7	2.0		1.9	1.7	1.9	1.7	1.8	1.6
- 4	1.9	1.7	1.6	2.0	1.6	1.9	1.7	1.8	1.7	1.7	1.7
- 3	1.8	1.7	1.8	2.1	1.7	2.0	1.8	1.9	1.7	1.6	1.5
- 2	1.7	1.5	1.7	2.0	1.8	1.5	1.7	1.8	1.7	1.8	1.5
- 1	1.7	1.7	1.6	1.8	1.7	1.7	1.7	1.8	1.7	1.8	1.5
Day of Delivery	1.7	1.7	1.7	2.0	1.7	1.8	1.7	1.8	1.5	1.7	1.4
1 Day Post-Partum		1.7	1.6		1.7	1.7	1.7		1.7		1.5

* Albumin concentrations in gm. %. ** - days are days pre-partum

Jugular Levels of Cholesterol* of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 19

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	381
-39**										63	
-38										65	
-37										74	
-36										75	
-35										75	
-34										80	
-33										78	
-32										75	
-31										51	
-30										48	
-29										67	
-28									60	64	
-27									70	65	
-26									80	70	
-25									77	60	
-24									89	65	
-23									82	66	
-22									97	70	
-21									85	70	
-20								55	76	66	
-19								59	76	70	
-18								60	59	65	
-17								70	55	64	50
-16								65	71	64	54
-15								66	78	65	59
-14								75	80	60	59
-13								70	75	60	61
-12								64	76		59
-11								63	51	65	64
-10								64	75	65	51
- 9							46	43	76	70	65
- 8							40	45	71	63	57
- 7		65		59		46	50	61	77	69	55
- 6	55	65		55		43	60	64	55	76	80
- 5	60	64	59	57		70	60	75	72	80	46
- 4	54	80	60	65	57	65	56	52	70	69	73
- 3	60	81	61	71	60	56	60	60	70	66	65
- 2	65	77	75	40	62	45	62	50	70	80	63
- 1	72	77	75	66	69	40	56	50	60	76	60
Day of Delivery	71	71	76	60	59	44	40	46	55	74	60
1 Day Post-Partum		67	75		55	43	50	43	67		57
2 Days Post-Partum									67		55

* Cholesterol concentrations in mg. %. ** - days are days pre-partum.

Jugular Levels of Bilirubin*of Pregnant Ewes Infected with

Listeria monocytogenes and in Normal Control Ewes.

Table 20

	Infected Ewes							Control Ewes			
Day	341	342	343	344	352	370	381	354	355	356	381
-39**										.11	
-38										.18	
-37										.29	
-36										.40	
-35										.35	
-34										.30	
-33										.40	
-32										.22	
-32										.11	
-30										.19	
-29									.10	.20	
-28									.22	.11	
-27									.30	.10	
-26									.35	.30	
-25									.24	.30	
-24									.38	.27	
-23									.30	.15	
-22									.39	.29	
-21									.19	.23	
-20								.16	.20	.22	
-19								.19	.19	.12	
-18								.30	.10	.20	
-17								.43	.18	.20	
-16								.31	.30	.30	.12
-15								.40	.28	.28	.22
-14								.15	.25	.30	.30
-13								.40	.10	.20	.22
-12								.15	.25	.30	.25
-11								.21	.27	.16	.22
-10								.16	.15	.20	.19
- 9							.16	.19	.24	.10	.20
- 8							.18	.20	.30	.12	.20
- 7		.27		.45		.20	.30	.24	.22	.20	.20
- 6	.22	.30		.49		.12	.29	.20	.23	.15	.10
- 5	.40	.40	.03	.31		.29	.30	.22	.22	.10	.19
- 4	.36	.39	.43	.39	.60	.60	.20	.14	.15	.20	.11
- 3	.40	.58	.42	.79	.30	.50	.40	.28	.30	.13	.21
- 2	.60	.45	.40	.42	.39	.20	.35	.10	.18	.10	.10
- 1	1.00	.60	.62	.31	.32	.20	.20	.55	.10	.15	.10
Day of Delivery	.90	.40	.42	.32	.33	.30	.40	.21	.19	.20	.10
1 Day Post-Partum		.45	.42		.40	.23	.29	.32	.22		.11
2 Days Post-Partum								.11			.11

* Concentration of Bilirubin in mg. %. ** - days are days pre-partum.

Rectal Temperatures of Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes.

Table 21

Day	Infected Ewes														
	341	342	343	344	346	347	348	349	350	351	352	340	345	339	357
1*	104.0**	104.5	105.0	105.8	103.0	103.4	104.4	103.8	102.5	103.2	104.0	105.2	104.0	104.2	103.6
2	103.0	105.0	104.4	105.8	105.2	107.0	105.6	105.4	102.4	103.4	103.4	102.5	104.0	102.4	104.2
3	106.0	105.2	106.2	105.4	105.0	106.5	105.8	104.0	104.6	104.6	102.4		103.0	102.8	104.2
4	104.4	103.8	103.6	102.0	106.2	106.2	103.0	103.4	103.4	105.0	103.4		102.0	103.4	101.2
5	103.0	102.0	102.4	102.2	103.0	103.4	102.4	102.5	101.4	101.8	102.2				101.5
6	102.6	102.4	102.4	103.0	102.4	102.5			101.6	101.8	102.0				101.4
7	102.8	103.0	103.2	102.2	103.4	102.4			101.6	101.5	101.2				101.5
8	102.0	102.2	102.4	102.2	104.0	104.0			102.0	101.5	102.0				102.0
9		102.4	102.6	102.2							101.0				102.0
10		102.2	101.6	102.4							102.0				102.4
11		102.0	101.6	102.4											101.4
12		102.0		104.2											102.2
13		102.0		102.0											101.6
14		102.6													102.0
15															101.6

* Day of Inoculation ** Degrees Fahrenheit.

Rectal Temperatures of Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes.

Day	Infected Ewes														
	358	359	360	361	362	364	365	366	367	368	369	370	371	372	373
1*	104.4**	103.8	104.4	104.2	103.8	104.2	104.4	105.0	105.2	104.6	105.0	102.5	103.4	102.0	103.6
2	104.0	104.0	104.4	104.0	105.2	102.4	102.0	102.4	102.5	102.2	102.6	105.8	102.4	104.2	104.4
3	103.4	105.4	103.4	102.2	103.4	104.6	103.6	102.4	104.4	104.0	106.4	105.4	104.4	104.2	105.0
4	10225	104.0	102.2	101.5	102.0	104.4	102.8	106.2	104.4	102.0	103.8	102.6	101.6	101.4	101.8
58	102.0	101.2	101.5	101.5	102.2	103.0	102.2	104.0	103.8	102.0	102.2	101.4	102.4	101.6	102.0
6	101.4	101.4	102.0	101.2	102.2	101.4	101.5	101.6	102.0	102.2	102.0	101.5	102.4	102.4	102.0
7	101.5	101.8	101.5	101.8	102.0	100.6	101.6	102.0	101.6	102.0	101.6	102.2	102.2	102.2	102.2
8	101.4	102.0	102.4	102.0	102.4	102.4	102.0	103.5	102.0	102.0	101.6	102.2	101.4	102.6	100.5
9	102.0	101.4	101.6		102.4	101.6	101.2	103.0	101.4	101.2	101.2	101.4	102.8	102.8	102.0
10	102.2	101.8	101.6		102.4	101.6	101.2	103.0	101.4	101.2	101.2	101.4	102.0	102.0	102.0
11	102.4	102.0	101.5		102.8	102.0	102.0	101.8	101.6	101.6	101.0	101.6	101.0	101.0	102.6
12	102.8	102.2	103.2		103.4		102.2	102.0	102.2	101.4	101.8	102.4		101.6	102.5
13	103.2	101.0	101.8		102.0		102.4	101.2	101.8	101.2	101.8			103.0	102.6
14	104.0	101.4	101.0		102.6		102.0	104.0	102.6		101.4			101.8	102.4
15	103.0	101.0	101.4		102.8		102.8	103.5	102.4		102.4			104.0	102.4
16	103.6	101.5	102.2				101.6	103.8	102.2		102.8			103.2	102.4
17	103.8	101.0	101.2				101.8	103.0	102.8		104.0				
18	104.0	101.2	101.8				102.2	104.2	101.5		102.8				
19	101.8	102.2	101.8					103.0	102.4						
20		101.8	102.5						101.5						
21		102.4	102.0						103.8						
22		101.0	102.5						102.0						

* Day of Inoculation ** Degrees Fahrenhhit.

Rectal Temperatures of Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes.

Day	Infected Ewes														
	375	376	378	379	380	381	382	382	384	385	386	387	388	389	390
1*	102.5**	103.2	103.4	104.0	103.4	103.6	102.6	103.4	102.8	102.2	101.6	104.0	101.8	102.2	103.0
2	104.2	104.4	104.6	105.4	105.0	106.2	102.4	104.6	103.2	102.6	103.4	102.2	102.0	102.0	102.6
3	106.5	105.6	104.5	106.4	105.0	104.6	103.6	104.8	103.0	103.6		102.4	101.6	101.8	101.6
4		102.4		102.8	101.6	101.6	101.2	103.8		105.8	1	104.4	102.6	102.4	102.8
5		101.8		102.0	101.2	102.6	101.4	103.0		101.8		103.2	103.8	105.2	102.4
6					101.6	101.4	101.6	103.2		101.0		102.0	102.6	104.0	104.0
7					101.5	101.8	101.4	102.5				101.8	103.4	103.8	104.0
8					101.4	101.2		102.6				101.8	102.2	101.0	101.6
9						101.6		102.8				102.0	101.2	101.5	101.0
10						102.4						101.8	101.0	101.6	101.8
11						101.8						103.2	102.4	104.4	104.4
12						102.4							102.0	101.0	101.6
13						102.4							102.6	102.2	102.[illegible]
14						103.8							102.8	102.0	102.0
15						101.4								[illegible]	102.2
16						103.0									102.0
17						102.0									102.0
18						101.0									
19						101.4									

*nDay of inoculation ** Degrees Fahrenheit.

Rectal Temperatures of Pregnant Ewes Dmfected with Listeria monocytogenes and in Normal Control Ewes.

	Infected Ewes						
Day	393	394	395	396	397	398	353
1*	102.6**	103.6	102.4	103.4	104.6	104.0	102.0
2	102.8	103.0	104.0	104.6	104.6	105.6	103.0
3	103.0	104.0	105.0	105.4	102.0	106.0	103.0
4	105.0	102.8	102.6	102.0	102.6	102.0	103.0
5	104.5	101.6	102.0	101.6	102.0	101.5	102.6
6	101.6	101.4	101.4	101.0	103.0	101.4	101.6
7	103.4	103.8	104.0	102.0	101.2	101.7	101.4
8	102.0	101.0	101.2	101.4	102.6	102.2	102.0
9	104.2	102.2	101.2	101.0	102.4	101.6	102.0
10	101.8	101.2	101.2	101.6	102.6	101.2	101.6
11	10202	102.6	101.2	101.0	102.4	101.6	102.0
12	103.6	102.0	101.4	101.6	103.4	101.4	102.0
13	102.2	102.4	101.4	101.8	102.4	102.0	102.0
14		102.0	101.2	101.4	102.0	102.0	101.4
15		101.0	103.0	101.0	102.0	102.0	101.0
16		101.8	002.8	101.4	102.0	101.6	102.0
17		101.2	103.2	101.2	101.0	101.4	101.6
18			103.4				101.0
19			101.8				102.0
20			101.0				101.1
21			101.2				101.0
22							101.2
23							101.0
24							101.2
25							101.8

* Day of Inoculation ** Degrees Fahrehheit.

Rectal Temperatures of Pregnant Ewes Infected with Listeria monocytogenes and in Normal Control Ewes

Day	353	354	355	356	374	391	Day	353	354	355	356	391	Day	355	356
								Control Ewes							
1*	104.2**	105.2	104.0	104.4	102.4	102.4	26	102.6	102.0	102.0	101.8	104.0	51	101.2	101.6
2	102.0	102.2	102.0	101.8	102.0	102.2	27	101.0	101.2	101.0	101.2	103.6	52	102.2	101.8
3	101.6	101.8	102.0	101.6		102.0	28	102.0	101.2	101.8	102.0	102.4	53	101.0	101.2
4.	101.2	102.0	102.0	101.0		102.8	29	101.2	102.0	101.0	101.6	102.4	54	101.8	101.0
5.	102.0	102.2	102.2	102.0		101.4	30	102.0	102.0	101.4	101.4	102.2	55	103.4	101.2
6	101.4	101.6	102.0	102.0		101.2	31	101.4	101.6	101.4	101.4	102.0	56	102.8	101.0
7	102.0	101.0	101.4	101.6		102.0	32	101.8	101.8	101.6	101.6	101.6	57		101.4
8	102.0	102.0	101.6	102.0		101.6	33	101.0	101.2	101.4	101.4	101.2	58		101.6
9	101.2	102.0	101.6	102.0		102.2	34	101.0	102.0	101.6	101.6	101.4	59		102.0
10	101.8	102.0	101.6	102.0		102.2	35	101.8	101.4	101.4	101.2	101.2	60		101.8
11	101.6	101.8	102.0	102.0		101.5	36		101.6	101.6	101.6	101.2	61		101.6
12	101.4	102.0	101.2	101.4		101.8	37		101.6	101.0	101.0	101.2	62		101.8
13	101.4	102.4	101.2	101.4		101.8	38		101.6	101.2	101.4		63		101.6
14	101.2	101.8	101.0	101.4		102.0	39		101.2	102.5	102.2		64		101.6
15	101.0	101.2	101.8	102.0		101.4	40		102.8	101.0	101.4		65		101.0
16	101.0	101.8	101.4	101.4		101.6	41		102.0	101.4	101.2		66		101.2
17	101.2	101.4	101.4	101.4		101.0	42		101.6	101.8	101.4		67		101.0
18	102.0	102.2	101.2	102.0		101.2	43			102.5	102.2		68		101.0
19	102.0	101.0	101.4	101.0		101.2	44			101.0	101.2		69		101.0
20	102.0	101.4	101.2	101.4		101.6	45			102.0	102.6		70		101.2
21	102.1	101.8	101.5	102.0		101.4	46			101.0	101.2		71		100.8
22	102.0	102.0	101.4	101.8		101.0	47			101.4	101.8		72		101.0
23	101.6	102.0	101.6	101.2		101.4	48			101.0	101.0				
24	102.0	101.4	101.0	101.0		101.8	49			101.0	101.4				
25	101.2	101.2	103.0	101.0		101.4	50			101.2	101.6				

* Day of Inoculation ** Degrees Fahrenheit.

CLINICAL-PATHOLOGICAL AND ENDOCRINE CHANGES IN THE SERUM OF EWES ABORTING DUE TO LISTERIA MONOCYTOGENES

by

James L. Carter

B. S., Kansas State University, 1971
D. V. M., Kansas State University, 1973

AN ABSTRACT OF A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

GRADUATE PATHOLOGY GROUP

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1976

Endocrine and clinical-pathological changes were measured in pregnant ewes infected with Listeria monocytogenes and in normal control ewes at abortion or parturition. Rectal temperatures were also taken.

Progesterone decreased in both groups at abortion or parturition. Estradiol and cortisol of the control ewes had a markedly increased level at parturition. The infected ewes had significantly increased levels of cortisol for 3 days after inoculation, but it returned to pre-inoculation levels for the remainder of gestation. Serum levels of cortisol did not change and estradiol levels increased only slightly at abortion by infected ewes.

The major clinical-pathological changes were the changes in the calcium, phosphorous, and glucose levels. The other parameters showed only slight changes which were not statistically significant. A decrease in serum calcium and an increase in serum phosphorous were noted in the control ewes at 1 day post-partum. An increase in glucose was observed in the control ewes following delivery. The serum alkaline phosphatase of the controls did not increase and decreased the day after parturition to below pre-parturition levels, but the serum alkaline phosphatase increased on the day of parturition in the test ewes. Cholesterol gradually decreased in the controls until two days post-partum and then increased. The test ewes had consistently higher levels of total bilirubin, lactic dehydrogenase (LDH), and serum glutamic oxalacetic transaminase (SGOT) than the controls, but the controls had higher levels of uric acid. The white blood cell numbers were increased after inoculation in the test ewes, with an increase in the percentage of neutrophils after inoculation and at abortion. No significant changes were noted in serum albumin and serum blood urea nitrogen (BUN). The packed cell volume, hemoglobin concentration and red blood cell numbers showed no pattern.

An increase in rectal temperature was observed in the test ewes after inoculation. This increase was not observed in the controls.