POSTPARTURIENT BOVINE UTERINE MOTILITY

FOLLOWING EXPERIMENTALLY PRODUCED

RETAINED PLACENTA

Ву

JOHN HOWARD VENABLE

Doctor of Veterinary Medicine Oklahoma Agriculture and Mechanical College Stillwater, Oklahoma 1953

the Oklahoma Agriculture and Mechanical College in partial fulfillment of the requirements for the degree of MASTER OF SCIENCE August, 1956

.

Administratistical college LIBRARY JAN 2 195 7

POSTPARTURIENT BOVINE UTERINE MOTILITY

FOLLOWING EXPERIMENTALLY PRODUCED

RETAINED PLACENTA

Thesis Approved:

25 Thesis Adviser 41.5. Mencome Mader 110

Dean of the Graduate School

ACKNOWLEDGMENTS

The writer wishes to express his gratitude to his faculty adviser, Dr. Leslie E. McDonald for the guidance and interest he has extended in planning and completing this study.

To the staff members of the Department of Physiology and Pharmacology, the Dairy Department and the Department of Veterinary Medicine and Surgery at Oklahoma A. and M. College the writer wishes to extend his appreciation for their full co-operation in supplying animals, equipment and facilities.

The writer wishes to extend his thanks to Mrs. Ruby Burns for her service in preparing the histological sections and to Mrs. Marilyn Johnston for her aid in typing.

To his wife, Pat, the author wishes to acknowledge his greatest indebtedness for her understanding and encouragement during this study and for her hours of patient assistance in producing this thesis.

TABLE OF CONTENTS

						Page
INTRODUCTION .		• • • •	• • • •	• • • •	• • •	1
REVIEW OF LITER	ATURE .	• • • •	• • • •	• • • •	• • •	2
U terine Mo R etained F	Placenta	• • • •	• • • • •	• • • •	•••	2 8
MATERIALS AND M	ETHODS	• • • •	• • • •		• • •	14
Recording Recordings Recordings Establishm Histologic The Sulfa-	Procedure From Nor ment of the cal Study	e rmal Ar he Expe of the	nimals Primental Placent	Group . omes .	• • •	
RESULTS	• • • •	• • • •	• • • •	• • • •	• • •	22
Normal Bov Uterine Mc				••••	• • •	22
Group . Histologic Spontaneou The Effect	al Study is Abnorma	of the al Puer a-Urea	Placent periums and Pito	ome	• • •	31 38 39 41
DISCUSSION				• • • •		45
SUMMARY AND CON	NCLUSIONS			• • • •	• • •	53
New Contri Substantia Suggestion	ibutions ation of H ns for Fun	Existing Ther S	ng Data . Study	• • • •	• • • • • •	53 54 55
BIBLIOGRAPHY .						57

LIST OF TABLES

Tabl	.0	Page
I	Normal Postpartum Uterine Motility (Jordan)	5
	Normal Postparturient Uterine Motility	26
III	Uterine Motility in the Experimental Cow - First Three Postparturient Days	32
IA	Uterine Motility in the Experimental Cow - Fourth, Fifth and Sixth Postparturient Days	37
V	Uterine Motility in Two Naturally Occurring Cases of Retained Placenta	40
VI	The Effects of Sulfa-Urea and Pitocin on the Normal Puerperium	42

.

LIST OF PLATES

Plate		Page
I	Closed Air Recording System	15
II	Recording Equipment in Operation	16
III	Uterine Contraction Rates in Normal Cows	23
IV	Uterine Contraction Rates in Cows with Experimentally Produced Retained Placenta	•
V	Normal Uterine Motility Pattern	. 25
VI	The Effect of Nursing During a Normal Puerperium	29
VII	A Comparison Between the Motility Patterns of the Upper and Lower Segments of the Uterus	. 30
VIII	Uterine Motility Pattern in Experimentally Produced Retained Placenta	34
IX	The Effects of Sulfa-Urea and Pitocin Upon the Normal Puerperium	. 44

INTRODUCTION

Normal involution of the uterus and rapid recovery from the stresses and cellular changes present at the time of parturition are of extreme importance in the husbandry of cattle to insure maximum production and breeding efficiency. ith this in mind it is evident that any factor impeding normal uterine involution warrants careful study in an attempt to prevent or to correct the pathology involved.

Factors such as motility, proper hormone balance and ability to prevent and overthrow infection are all interrelated and known to be directly responsible for normal involution. In cattle, retained placenta extends the period required for normal involution and increases the incidence of uterine infection. The cause of the increased incidence of non-infectious placental retention in cattle is unknown but recently it has been suggested that a reduced uterine motility is associated with the condition.

The purpose of this study was to produce experimentally retained placenta by corpus luteum ablation and compare the postpartum uterine motility pattern of the experimental animal with that of the normal cow. A histological study of the placentomes in the experimentally produced retained placentae was included to observe any structural changes in the fetal- ternal attac nt.

REVIEW OF LITERATURE

I Uterine Motility

Uterine motility has been studied <u>in vivo</u> and <u>in vitro</u> using rabbit and human subjects predominantly (Reynolds, 1949). Csapo and co-workers (Csapo and Corner, 1951: Csapo and Goodall, 1954) have worked extensively on the physiology and biochemistry of myometrial contraction using uterine strips of rabbit origin.

Uterine muscle strips and intrauterine balloons have been used to study uterine motility in dairy cattle. Cupps and Asdell (1944) established a normal motility pattern for bovine myometrial strips obtained during various stages of the estrous cycle. They recorded small frequent contractions beginning during the last two days of proestrus. These contractions reached a peak during estrus and thereafter progressively diminished. Superimposed, small contractions appeared during estrus and persisted until the motility ceased at the eighth postestrual day. With this in <u>vitro</u> technique, pituitrin elicited prompt tonic contracture at all stages of the estrus cycle.

<u>In vivo</u> studies in dairy cattle have been confined chiefly to problems involving the estrous cycle. Evans and iller (1936) reported a motility experiment utilizing an

intrauterine balloon. They observed marked activity during estrus. This activity was maintained for two to three days following ovulation; a progressively decreasing contraction rate was then observed until the eleventh to sixteenth day. Increased activity became evident on the sixteenth to twentyfirst day and continued until maximum activity was again reached during the next estrus. Pituitrin produced myometri 1 spasm during estrus but the uterus became refractive to this oxytocic principal following ovulation. VanDemark and Hays (1951) showed the effects of oxytocin, epinephrine, breeding techniques and milking on the uterine motility of cows duri different phases of the estrous cycle by using an intrauterine balloon technique for recording contractions. Later, these workers (Hays and VanDemark, 1953), described the spontaneous motility of the uterus throughout the estrous cycle and the role of uterine motility in the transportation of spermatozoa at coitus. The recordings made during estrus demonstrated small contractions with high frequencies of four to four and one-half contractions per minute. During midestrus, the frequency of the contractions diminished but the amplitude increased along with irregular changes in tone. A lack of motility was demonstrated in ovariectomized cows, but the normal motility of estrus was re-established by the administration of estrogens. When progesterone was administered to these animals, the uterine contractions increased in amplitude but maintained a constant rate.

Rowson (1955) demonstrated uterine motility by placing

radio-opaque material in the uterus at estrus. This study was performed with the uterus extirpated and graphically showed the stimulatory effect of oxytocin during this phase of the estrous cycle.

Fitzpatrick (1954) used the intrauterine balloon technique to record the action of oxytocin and vasopressin upon uterine muscle during the estrous cycle. The ruminant uterus as responsive to both of these posterior pituitary fractions. The stimulation by vasopressin was chemically different from that of oxytocin in that it was dependent upon or affected by increased blood levels of magnesium. The effects of vasopressin appeared earlier than those of oxytocin but were not as powerful as the latter.

Postparturient bovine uterine motility studies have been confined to involution observations made by rectal palpation and by using the intrauterine balloon technique. Buch, Tyler and Casida (1955) collected statistical data concerning uterine involution in an experimental herd of Holstein-Friesian cows. They calculated a mean involution time of forty-seven days following all normal deliveries. Involutiontime was found to be significantly different in primiparous and pluriparous cows and in parturitions occurring during different seasons of the year. Pluriparous cows showed complete involution in fifty days as compared to a forty-two day average for primiparous individuals. Involution required longer periods during the winter and spring months than during the fall and summer.

An intrauterine balloon technique was used by Jordan (1953) to demonstrate <u>in vivo</u> bovine puerperal uterine contractions. Observations were made during parturient and postparturient periods on 107 cows and heifers that were free from brucellosis. Recordings of the contractions were inscribed upon an electrically driven kymograph. Fortythree recordings of the normal uncomplicated puerperium were observed and summarized in the following table:

TABLE I

NORMAL POSTPARTUM UTERINE MOTILITY

Hours post partum	No.of cases	No.of contr. per hour	Strength (mm.Hg)		Relaxation time-(mins.)
1-12	27	13.3	20.2	0.7	1.07
More than 12	16	7.9	13.6	0.6	1.20

Included in this study were several abnormal postparturient states including retained placenta, milk fever and abortion. Two animals in the herds under observation aborted. One recording was made three to four hours following abortion and the other, thirty-eight hours postabortion. In contrast to the normal puerperium, both showed moderate contractions of high frequency. Even the recording taken late in the puerperium showed contractions every two minute .

Three cases of retained placenta were observed. These record s were taken within three hours of birth in each

case. Uterine contractions were greatly reduced or entirely absent. From these observations, Jordan hypothesized that placental retention was associated with a reduced uterine motility during the first twenty-four hours following parturition.

Jordan's work also included a study of the effects of pituitary extract on seven normal and six abnormal puerperiums. In the normal animal, both the frequency and forc of the contractions were increased in the form of a tetanic spasm which subsided to large rhythmic contractions within four to nineteen minutes. In cases of retained placenta, the drug acted similarly but to a lesser extent. No appreciable effects were noted when pituitary extract was administered to a cow that aborted.

Uterine motility in the human female has been studied by the use of the intrauterine bag (Schatz, 1872) and external tocography (Reynolds, 1949). The intrauterine bag technique has been employed during the estrous cycle (Kurzrok, <u>et al</u>, 1937), labor and the puerperium. This technique lends itself well to the latter type of study.

Human puerperal uterine contractions ere recorded by Adair and Davis (1934). During the immediate postparturient period, strong contractions occurred approximately every five minutes. The recordings illustrated were markedly similar to the bovine recordings made by Jordan. These workers stressed the differences in the contraction patterns of the upper and lower segments of the uterus. Recordings

were presented which showed a highly active upper segment; but when the balloon was pulled back into the lower segment, a marked decrease in motility was recorded. The upper segment of the uterus was still active on the eighth postpart day. Pitocin, pitressin and pituitrin were used during this latter postpartum period and the same degree of uterine activity was produced by each.

Gardiner, prague and Bradbury (1940) showed that the human uterus exhibited only slight spontaneous activity between the sixth and ninth day following delivery. Pitocia, pitressin and pituitrin were administered in large doses during this period. Pitressin produced a slightly shorter period of uterine activation but the three drugs were other-

ise equal in action. Considerable variance was encountered in the patients' responses. Identical effects were produced by equal dilutions of the pitocin and pitressin samples; this finding demonstrated that the oxytocic effect could not be due to impurities. It was also shown that there is a difference in human and guinea pig response in regards to the oxytocic assay of pitocin and pitressin. Human patient also showed a non-specific decreased response to the second and third administrations of the drugs irregardless of the order given or the combinations used.

Bickers (1942) studied the human uterus over a fifteenday period following spontaneous childbirth. Following delivery, recorded contractions occurred every three minute and slowly decreased in rate and amplitude so that on the

fifth day, contractions occurred every four to seven minute . On the tenth postpartum day, motility was practically absent and was completely absent by the fifteenth day. The stimulatory effect of pitocin was marked following delivery but diminished in direct proportion to the loss of spontaneous motility. A direct relationship was established between the contraction pattern and the level of estrin in the blood. The administration of estradiol benzoate re-established the motility and the sensitivity to pitocin.

Greenberg (1946), in describing the first puerperal hour as the fourth stage of labor, indicated that during this period the uterus is apathetic and isotonic, especially if the first two stages of labor have been prolonged. No recorded data were presented to portray this point significantly.

It is interesting to note that a lack of uterine motility was cited as the etiology of 72.6 per cent of a group of human cases of retained placenta (Ranney and Yankton, 1945). The defect arose when implantation occurred in the uterine horn with a resulting pouching and thinning of the uterine wall until it became non-motile.

II Retained Placenta

Non-infectious bovine retained placenta was reported by Kennedy (1947) to occur in 8.3 per cent of animals from English herds where brucellosis was absent or "quiescent". Palmer (1932) and Boyd and Sellers (1948) reported retained

placentae in 11.7 per cent of 125 deliveries and 6.4 per cent of 450 deliveries respectively. These studies were also made in herds free from brucellosis. Fincher (1941) observed that approximately one-third of the cases of retained placenta presented to the Ambulatory Clinic at Cornell University could be attributed to brucellosis. He conceeds, however, that a large percentage of the cases was of unknown origin and lists many varied factors such as heritability and improper nutrition as contributing to this postpartum defect.

Williams (1943) was of the opinion that uterine motility was not a factor in placental retention. He quoted Pomayer (1908) in stating that the chief cause of uterine atony was prolonged dystocia. Conservative breeding was presented as the best preventative for non-infectious retained placenta.

Coid and McDiarmid (1954) reported that in a brucellosis free herd of 382 dairy cattle, 3.7 per cent retained their placentae for more than 72 hours postpartum. The author stated that the percentage would have been greater if an earlier criterion of 24 hours had been selected. One of the fourteen animals which ret ined was treated by manual removal of the placenta. The rest were treated only with parenteral injections of stilbesterol. The subs quent milk production and breeding histories of the normal animals and those whos placentae were retained and left intact ere compared. No significant difference between the groups vas noted although the average butterfat production records were 365+ 89# for

the normal group as compared with $352\pm 55\#$ for the retained group. These observations indicated that retained placenta, while aesthetically undesirable, was not a severe detriment to the cow.

oore (1947) studied the blood picture of cases of retained placenta in cattle. These animals developed a uniform picture of toxic granulation and reduction of the neutrophiles, typical of a toxemia. This worker concluded that a high percentage of the placental retentions ere not infectious in nature; the clinical manifestations being due to toxic products of the degeneration of fetal membranes. The speed of recovery from the placental retention was directly dependant on the rapidity of involution and the resultant reduction of absorption from the uterine lumen.

Stewart (1943) published his observations concerning clinical retained placentae and emphasized the necessity for manual removal of the fetal tissues. He suggested that the rupture of the umbilical vessels and the subsequent los of blood pressure in the chorio-allantoic membranes were th primary factors in loosening the fetal-maternal attachment.

Pomayer (1919) presented an hypothesis similar to Stewart's and noted that retention of the fetal membranes occurred most frequently in cases of uterine inertia due to infection, debility or premature birth.

Vinding (1955) presented an opposing hypothesis concerning the etiology of non-infectious retained placenta. He stated that a majority of cows so afflicted had delivered

their calves while in a standing position and therefore, the weight of the calf placed excessive tension on the chorioallantoic membrane. This tension was believed to produce obstruction to the normal venous drainage of the caruncles and possibly partial eversion of the pregnant uterine horn with resulting venous embarrassment. Edema of the caruncle resulted and the chorionic villi were trapped in the closing maternal crypts. Degenerative changes, accompanied by connective tissue proliferation, rapidly prevented any further possibility of a normal separation. The author stated that in over 10,000 deliveries, where he was present to prevent excessive tension of the fetal membranes and where the uterus was placed in a normal position following delivery, no cases of non-infectious retained placenta were reported.

McDonald, <u>et al.</u> (1954) experimentally produced placental retention in the cow by ablation of the corpus luteum. Seven of the eight cows in the experimental group delivered before the expected delivery date of 278 days (Jafar, <u>et al.</u> 1950). Six of these seven ani als delivered outside one st ndard deviation from the mean delivery d te. Prevention of the experimental retention w s accomplished in another group by the administration of progesterone during the last sixteen to twenty-nine days of the gestation period. All injections were discontinued by the t o hundred seventyeighth day. All of the animals in this group delivered within one st ndard deviation of the expected date.

The histology of the bovine placentome was first reviewed by Hammond (1927). He classified the fetal-maternal union as syndesmochorial. A considerable amount of controversy arose as to the true state of the placental barrier. In fixed sections, a low cuboidal epithelium was seen lining the maternal crypts of the caruncles; it was separated from the trophoblast of the chorionic villi by an open space. This epithelium was described as maternal by Wimsatt (1953) and Hatch (1941) and if their hypothesis were true, the barrier was epitheliochorial. Foley and Reece (1953) described the cuboidal layer as fetal in origin. They hypothesized that these cells resulted from the migration of the cells of the trophoblast and agreed with Hammond's classification of syndesmochorial. Gordon (1949) injected a new concept as to the origin and function of the trophoblast when he presented indirect evidence that the trophoblast was of maternal origin, derived from the granulosa cells of the ovary.

The space that appears in fixed specimens between the fetal trophoblast and the cuboidal epithelium lining the uterine crypts was described by Weeth and Herman (1952) as an artifact which developed during the dehydration stage of the fixation. The variation in the dehydration in the maternal and fetal tissues was due to the wide differences in the water content of the two, therefore a mechanical separation occurred at the area of least cohesion. These workers described an aging process in the placenta during

pregnancy that consisted of an increased ratio of collagenous to reticular fibers.

Histochemical observations described by Foley and Reece (1953), Foley, <u>et al.(1954)</u>, Wimsatt (1953) and Weeth and Herman (1952) indicated a high chemical activity of the fetal-maternal barrier throughout pregnancy. The latter workers observed an alkaline phosphatase barrier in the cuboidal epithelium lining the maternal crypts.

At parturition, the maternal and fetal cotyledons degenerate rapidly. Weeth and Herman (1953) stated that within eight days, the maternal cotyledon was a degenerate mass and that necresis of the fetal membranes began within an hour following delivery.

Kennedy (1947) presented the only comparative histological picture of the placentomes of normal cattle and those of naturally occurring retained placenta. Thirty-one normal fetal and maternal cotyledons were examined that had been collected at an average time of four and three-quarter hours postpartum. Kennedy found the epithelium lining the maternal crypts to be distinctly visible in many cases but in others it was absent. The outlines of the maternal crypts were obliterated in some areas. Twenty-four placentomes from cases of retained placenta were examined but no observable differences were noted.

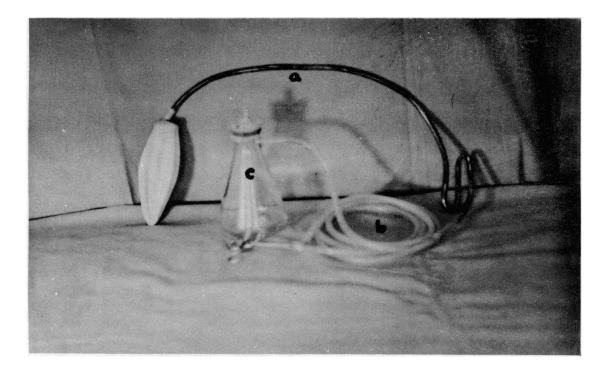
MATERIALS AND METHODS

The immediate problem faced in initiating this study of uterine motility was selecting a physical method of recording uterine contractions. An intrauterine balloon technique was selected for the practical reason of availability of equipment.

Several pilot recordings were made, using various designs of equipment, on postparturient animals. The greatest difficulty arose in maintaining the equipment within the uterus and adapting the balloon to variables. such as the amount of intrauterine air and the degree of uterine involution. Water systems and air systems were compared on The closed air system was found to be as several animals. sensative as the closed water system and easier to use. Tho equipment selected for the collection of data is pictured in Plates I and II. The balloon was a four inch rubber beach ball with sides of greater elasticity than the tambour that activated the writing lever. Tygon tubing was used to convey the changes in air pressure to the tambour. Recordings were traced on an electrically driven kymograph. The intrauterine portion of the Tygon tubing contained a two and onehalf foot length of one-eighth inch copper tubing. The metal tube was pliable but aided in maintaining the system along the normal curvature of the uterine horn, thus



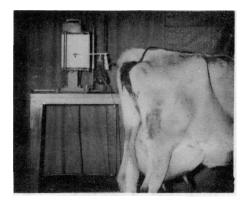




a. Intrauterine segment; Rubber beach ball, 4" diameter.
3/8" Tygon tubing covering a piece of malleable 1/8" copper tubing.
b. Interconnecting Tygon tubing with outlet for the introduction and release of air.
c. Recording tambour.

PLATE II

RECORDING EQUIPMENT IN OPERATION





- a. Reservoir pen; Gorrell and Gorrell, Haworth, New Jersey
 b. Balsa wood writing arm
 c. Recording tambour; Rubber sheeting placed over the
 - mouth of a vacuum bottle, Cork activator glued to the top of the rubber tambour.

assisting in holding it in place. Recording periods were not begun until after the second postpartum hour since great difficulty was encountered in maintaining the equipment in the uterus immediately following parturition due to the size of the organ, the rapid involution following the expulsion of the fetus and the persistant straining that was often encountered.

Recordings were made with the cow stanchioned. The tail was restrained away from the vulva and the entire perineal region was scrubbed with soap and water and rinsed with various common antiseptic solutions, all of which proved adequate or perhaps unnecessary. The area was draped with sterile shrouds during early recordings but as technique improved, this procedure was discontinued without incidence of metritis in the normal group. The intrauterine segment of the recording equipment was chemically sterilized and manually placed in the recently pregnant horn with a sterile sleeve covering the arm and hand. The air system was left open for a period of five minutes to allow the balloon to adjust to the shape and size of the uterine lumen. During this period a balance was reached between the negative abdominal pressure, the uterine tone, the elasticity of the sides of the balloon and the atmospheric pressure. Under normal conditions, the amount of air drawn into the balloon was less than fifty cubic centimeters. The system was attached to the rubber tambour and contractions recorded for varying periods between thirty minutes and three to four hours.

Additional air had to be added on occasion to obtain an interpretable recording and the balloon's large potential size aided in this adjustment without increasing the intraballoon pressure too radically. These adjustments were necessary where the uterine lumen had a large potential siz or where the uterus was inflated. The crit rion used in determining the amount of air placed in the balloon was the size of the inscriptions of normal respiratory movements on the kymograph. From experience it was found that if respiratory movements were recorded, uterine contractions, if present, were also recorded. If respiratory movements were not recorded, it was found that small contractions were missed or were recorded at such low magnitude that doubt persisted as to their validity when the tracings were studied.

It is acknowledged that the amount of air in the balloon greatly affected the recorded force of contractions. For this reason, studies were largely confined to the rate of contractions since this apparently was not affected by the varying amounts of air used in the balloon during this study. In general, the amount of air in the balloon was between twenty-five and one hundred cubic contimeters. The baselin pressure varied from a minus five to a plus ten millimeters of mercury unless otherwise specified.

Statements have been made in this study concerning the amplitude of the contractions but these were subject to the uncertainty of the amount of air in the balloon and have be n

confined only to points where the writer considered conditions comparable.

The first study was to establish the contraction rate during the normal puerperium. Recordings were made from postparturient cows in the Oklahoma A. and M. College dairy herd. The tracings were made at variable times between two and forty-two hours postpartum. Recordings were divided into thirty minute intervals and each interval was studied in terms of rate, amplitude and duration of contractions. Multiple recordings were made on several of the minoteen animals used in the study with a total of thirty recordings.

The second study consisted of making postparturient tracings from six animals whose corpora lutes were removed between the two hundred fifteenth and the two hundred fortysecond day of gestation. Removal of the corpus during this poriod was designed to produce experimental placental retention without producing abortion. Relatein-Priesian cova wore used for the experiment and wore purchased from local dairymen. All vero pluriparous, dry and negative to a serva agglutination test for <u>Grucella</u> abortus. They were collected into one pasture and maintained on a dist of prario hay, alfelfa hay and available winter pasture. None of the animals showed signs of disease other than that produced experimentally. The corpora lutes were removed by the intravaginal routs described by Halonald (1952). One abortion followed corpus ablation on the fourth postoperative day. The remaining five animals showed no ill offects from the surgery.

Following delivery, the experimental animals were stanchioned and recordings were made using the same technique employed in the normal group. Recordings were made daily for a period of six days. During the first three days, no treatment was administered to the animals even when the placenta was retained. Pilot experiments were begun on the fourth postparturient day and recordings were made of the uterine motility pattern associated with this three-day experimental period. These experiments included various standard treatments for retained placenta.

The third study entailed histological comparison of the placentomes of the experimental cows with those of the normal. For the first three postparturient days, whole placentomes were excised without disturbing the attached fetal tissue. These specimens were taken following each recording. The placentomes were cut, fixed in ten percent formol-saline, embedded in paraffin and sectioned at six microns. The tissues were stained with Harris-hemotoxylin and counterstained with eosin bluish. Slides were examined for the purpose of eliminating the possibility of infectious placentitis and for observation of the maternal placental attachment in the experimental group.

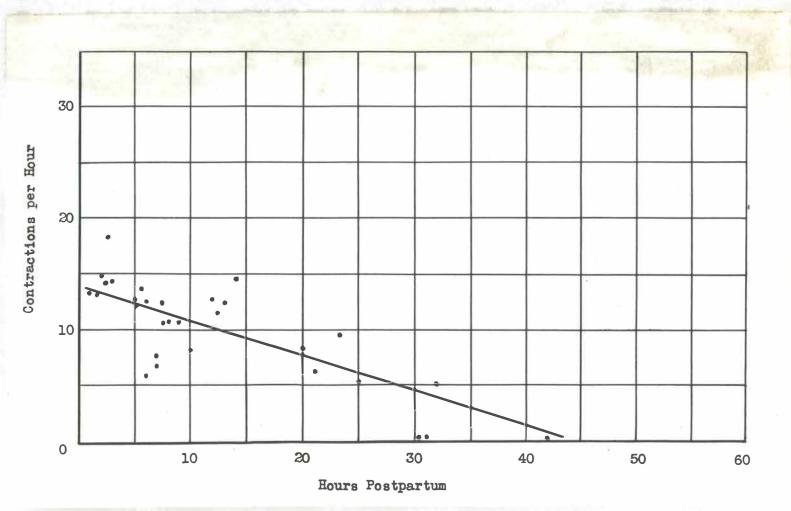
The fourth experiment was designed to show the effects of a sulfonamide-urea preparation on postparturient uterine contractions. Four brucellosis-free dairy cows, three Jerseys and one Jersey-Guernsey cross, were purchased while dry and placed on a native pasture to await delivery.

Following parturition, a normal tracing of the uterine contractions was made. As soon as the normal pattern was exhibited, four sulfa-urea bolets (Pitman Moore Co.) were Each bolet contained two hundred placed in the uterus. twenty grains of urea, thirty grains of sulfanilamide and five grains of sulfathiazole. The tracings were continued for one hour following the drugs administration. A second tracing was made approximately twenty-four hours after delivery to note subsequent deviations from the normal contraction pattern. After this latter pattern was established, the animal was treated intramuscularly with twenty units of pitocin (Parke-Davis Co.) and the tracing continued as long as necessary to record the effects. Following the thirtysixth postpartum hour, constriction of the cervix usually prevented further introduction of the equipment into the uterus.

RESULTS

I Normal Bovine Uterine Motility

The puerperal motility pattern of the normal group of dairy cows was characterized by rhythmic contractions that occurred at an average initial rate of fourteen contractions per hour. This rate diminished as the puerperium progressed until at forty-two hours postpartum the average contraction rate was less than one contraction per hour. During the first few hours of the puerperium, the contractions were strong, producing pressures between twenty and forty millimeters of mercury. Pain accompanied each contraction and was evidenced by a rapid shifting of the hind feet. As the contraction rate subsided, so too did the strength of the contractions so that at the forty-eighth postpartum hour. motility was indiscernable except for irregular changes in uterine tone. Graphic representation of the contraction rate during the normal puerperium is presented in Plate III. A reproduction of a typical normal recording is presented in Plate V. The contractions of each normal cow are tabulated in Table II. The contraction time did not vary markedly throughout the first thirty-two hours of the puerperium. An average contraction lasted from one to two and one-half minutes. Long contractions of three to four minutes were



UTERINE CONTRACTION RATES OF NORMAL COWS

PLATE III

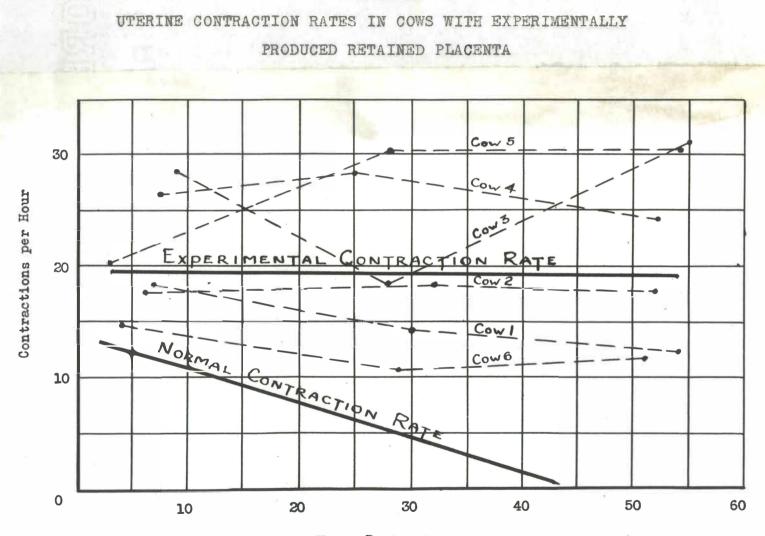


PLATE IV

Hours Postpartum

PLATE V

NORMAL UTERINE MOTILITY PATTERN

- a. Primary Uterine Contraction c. Small Respiratory Movements
- b. Skeletal Muscle Movements d. Smooth Muscle Contractions
- b'. Straining

of Unknown Origin

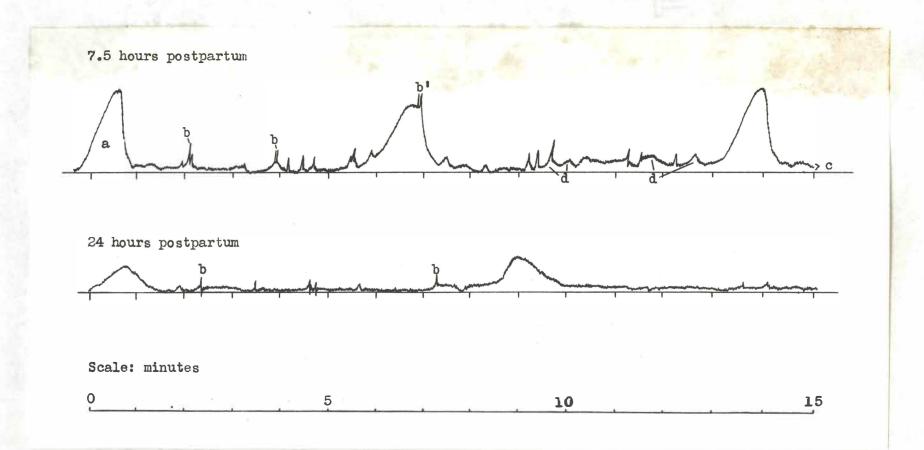


TABLE II

NORMAL POSTPARTURIENT UTERINE MOTILITY

	an a					an an Al Malandaria an an ann an Alin an Alina bha
MoC	Breed of Cow Sex of Calf	Gestation Length	Hours Postpartum	Aver.Time Between <u>Contr.</u> Range (in min.)	Aver. Length of Contr. Range (in min.)	No. of Contr. Hour
3	Hol.	unkn.	5.00	<u>4.94</u> 1.5-8.0	1.98 1.5-2.2	12.14
4	Jer.	unkn.	24.00	6.18 3.0-9.0	2.2	9.70
5	Hol.	unkn.	9.00	5.60	1.54 1.0-2.5	10.71
6	Jer.	278	1.5	4.58	$\frac{1.98}{1.0-2.7}$	13.10
			2.5	<u>4.11</u> 3.0-5.1	1.65	14.60
7	Hol.	unkn.	12.0 0	4.62	$\frac{1.78}{1.2-2.3}$	12.99
			12.5	<u>5.1</u> 2.1-7.4		11.76
			13.5	<u>4.81</u> 3.0-6.5		12.47
8	Hel. M	unkn.	•75	4.55	$\frac{1.95}{1.7-2.5}$	13,18
9	Hol. M	unkn.	2.00	4.07	$\frac{1.85}{1.2-3.0}$	14.74
	· .		20.00	<u>7.15</u> 6.0-9.0	<u>2.17</u> 2.0-2.3	8.39
			21.00	9.13		6.57

TABLE II (continued)

CO	Breed of Cow	Sex of Calf	Gestation Length	Hostpartum	Aver.Time Between <u>Contr.</u> Range (in min.)	Aver. Length of Contr. Range (in min.)	No. of Contr. Hour
11	Guer.	(in 1	288	6.00	$\frac{10.00}{7.0-14.9}$	<u>1.73</u> 1.3-2.2	6.00
				6.7	<u>8.80</u> 8.0-10.0	- · .	6.90
				31.00	Less than	one contr.	per hour.
12	Jer.	212	279	14.00	<u>4.07</u> 3.5-4.5	2.22	14.75
				25.00	<u>11.25</u> 10.5-12.5	2.37	5.33
13	Guer.	F	286	2.5	<u>3.25</u> 3.0-4.0	$\frac{1.83}{1.5-2.0}$	18.46
				7.25	<u>4.85</u> 4.1-5.8	<u>2.20</u> 1.7-3.1	12.37
				7.5	5.0-0.2		10.83
14	Jer.	13,	unkn.	6.0	4.78	<u>2.19</u> 1.5-2.0	12.55
16	Guer.	Fin 1	288	5.0	<u>4.83</u> 3.7-5.7	1.45 1.2-1.7	12.42
				30.33	Less than	one contr.	per hour.
17	Arys.	M	280	42.0	Less than	one contr.	per hour.
18	Guer.	P	288	10.0	7.06 6.33-8.1	1.84 1.2-2.4	8.50
19	Jør.	<u>a</u>	289	8.0	<u>5.95</u> 4.0-7.7	$\frac{1.7}{1.7-1.7}$	10.08
				32.00	$\frac{11.57}{6.75-16.4}$	<u>1.63</u> 1.0-1.7	5.18

found in the later hours of the puerperium and were low contractions which may not have been physiologically identical to the distinct, strong contractions found during the first twenty-four puerperal hours.

The rate and amplitude of the normal contractions were not affected by changes in the volume of air within the intrauterine balloon. The base line was raised on several occasions to twenty millimeters of mercury without eliciting a contraction or producing any noticeable difference in the contraction rate.

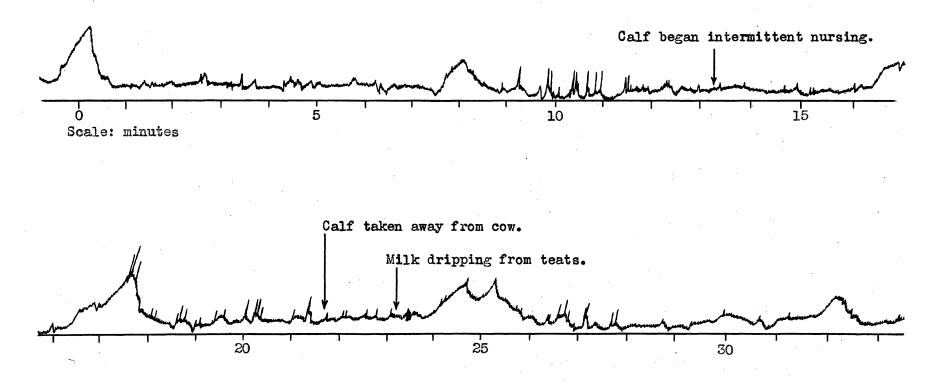
The calves were allowed to nurse during several of the recordings with slight and perhaps insignificant effect (Plate VI). The rate of contraction usually remained the same or exhibited an increase of one contraction per hour. When the calf was not allowed to nurse, consecutive recordings showed slight progressive decreases in contraction rate.

The state of excitement of the animal apparently had little effect upon the rate, initiation or inhibition of contractions; however, no severe excitement states were encountered in this study.

Motility recordings were made from the pregnant uterine horn but occasionally the balloon slipped back into the body of the uterus. In this area, contractions could be recorded only with the balloon greatly inflated. The region near the internal os of the cervix was less motile than the uterine hern. Plate VII demonstrates comparative recordings from these areas within the same cow.

PLATE VI

THE EFFECT OF NURSING DURING A NORMAL PUERPERIUM

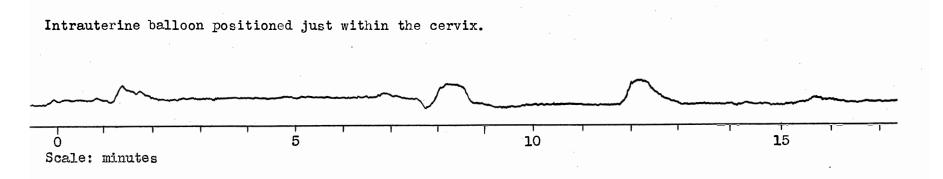


N

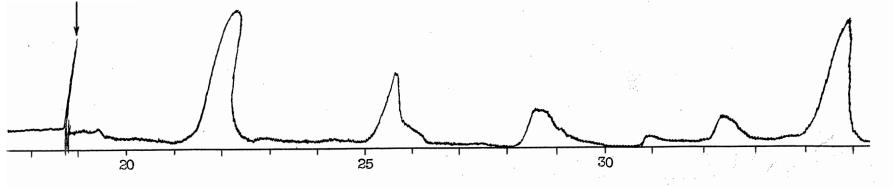
PLATE VII

A COMPARISON BETWEEN THE MOTILITY PATTERNS OF

THE UPPER AND LOWER SEGMENTS OF THE UTERUS



Intrauterine balloon positioned deep within the uterine horn.



II Uterine Motility of the Experimental Group

The motility pattern during the puerperium of the experimental group of Holstein-Friesian cows whose corpora lutea had been removed differed markedly from that of the normal group. Table III contains the tabulated data concerning the gestation, puerperium and uterine motility associated with these animals.

The first obvious differences exhibited by the group were the early parturition and the fact that all but one of the cows retained the placenta. This experimental placental retention was characterized by a lack of mucous discharge from the uterus and the hyperemic appearance of the fetal membranes. The cow that shed the placenta, did so within four hours following delivery. The set of the group retained their placentae until degeneration and liquifaction occurred or until the membranes were manually removed after the third postpartum day. Excluding the cow that aborted immediately fellowing corpus ablation, the average calving date for the group was 268.4 days.

The puerperal motility pattern is graphically compared with that of the normal group in Plate IV. The most notable abnormalities observed in the motility patterns of the experimental cows were: 1) the increased rate of contraction, 2) the prolongation of the contractility of the uterus over a three to seven day period, 3) the appearance of tetanic contractions and 4) the appearance of secondary, superimposed undulations. These four characteristics are shown in Plate VIII.

TABLE III UTERINE MOTILITY IN THE EXPERIMENTAL COW - FIRST THREE POSTPARTURIENT DAYS

Day 2

Day 3

Dav	1		

Cow	Rect. Temp. OF.	Hours Postpartum	State of Uterus	Aver.Time Between Contr. Range (in min.)	Aver. Length of Contr. Range (in min.)	of Contr. Hour	Amp. SHmm	Recto Temp.	Hours Postpartum	State of Uterus	Aver.Time Between Contr. Range (in min.)	Aver. Length of Contr. Range (in min.)		maxmin. w mmHg	$\operatorname{Rect}_{\delta_{F_{\bullet}}}$ Temp	Hours Postpartum	State of Uterus	Aver.Time Between Contr. Range (in min.)	Aver. Length of Contr. Range (in min.)	of Contr. Hour	maxmin.W mmHg du
1 Corpus removed, 242day. Calved, 274day.	102.5	7.0	Retained placenta Involution normal	3.32 3.0-4.1-	<u>2.20</u> 1.7-3.0-	18.07	40 20	102.2	30.0 31.0	Retained placenta Involution normal	<u>4.68</u> <u>3.4-6.2</u> <u>4.24</u> <u>3.0-5.7</u>	$\frac{2.53}{2.0-3.0}$ $\frac{2.64}{2.2-3.1}$	12.82 14.15	8	103.4	54.0	Placenta liquefied No further involution	4.98 4.0-6.0	3.25 3.0-4.0	12.05	20 9
2 Corpus removed, 221day. Calved, 266day.	102.4	6.3	Retained placenta Involution normal	3.40 2.5-4.2	1.61 1.2-2.0	17.65	30 20	102.8	32.0	Retained placenta Slight involution	<u>3.32</u> 2.6-4.3	2.03 1.4-3.0	18.07	40 20	103.6	52.0	Placenta degenerating No further involution	3.44 2.5-4.1	1.93 1.4-3.0	17.44	30 10
<u>3</u> Corpus removed, 215 day Aborted, 219day.	102.8	9.0	Retained placenta Involution normal	2.10 1.0-4.3	1.62 1.2-2.0	28.57	40 10	103.6	28.0	Placenta degenerating Marked involution	3.31 1.2-6.0	Accurate measure could not be made	18.13	25 3	102.6	55.0	Placenta liquefied Marked involution	$\frac{1.93}{1.0-5.0}$	1.27 0.9-1.9	31.08	25 10
Corpus removed, 236day. Calved, 253day.	102.5	7.5	Retained placenta Involution normal	2.29 1.5-3.2	1.72 1.4-2.2	26.20	40 20	103.5	25.0	Retained placenta Involution less than rormal	2.13 1.6-2.7	1.69 1.0-2.3	28.17	30 5	102.0	52.0	Placenta still intact Involution less than normal	2.48 1.6-3.0	1.83 1.5-2.0	24.19	40 10
5 Corpus removed, 231day. Calved, 275day.	102.5	3.0	Retained placenta Involution normal	2.96 2.0-4.0	1.61 1.2-2.1	20.27	25 5	102.8	28.0	Retained placenta No further involution	1.99 1.2-4.5	1.37 0.8-2.0	30.15	20 2.5	104.0	54.0	Placenta degenerating Slight involution	<u>1.95</u> 1.3-3.2	1.63 1.2-1.9	30.77	30 5
6 Corpus removed, 233day. Calved, 275day.	102.0	4.0	Placenta expelled Involution normal	4.06 2.8-6.3-	1.76 1.2-2.0-	14 . 78	35	101.2	29.0	Involution normal	<u>5.53</u> 4.4-6.2	2.21 2.2-3.3	10.84	40 30	101.2	51.0	Involution normal	5.05 4.3-5.5	1.5 1.0-2.0	11.88	30 10

PLATE VIII

UTERINE MOTILITY PATTERN IN EXPERIMENTALLY

RETAINED PLACENTA

cow 4

Corpus luteum ablated on the 236th day of gestation.

Parturition occurred on the 253rd day.

a. Primary uterine contraction

b. Skeletal muscle movements; coughing, lowing and straining

c. Development of tetany

- d. Secondary, superimposed undulations
- e. Tetanic contractions
- f. Negative uterine pressure is a reflection of the negative abdominal pressure.

W W

7.5 hours postpartum a C 52 hours postpartum 102 hours postpartum 103 hours postpartum 30 units pitocin е 30 minutes following pitocin e 10 15 5 0 Scale: minutes

On the first postparturient day, the cow that expelled the placenta in a normal manner (Cow 6) exhibited a contraction rate comparable to a normal cow. On the second and third postparturient days, this animal continued to produce a high frequency of contractions unlike the pattern established by the normal group. The other experimental cows developed initial contraction rates well above the normal and all maintained this increased rate beyond the third puerperal day.

Except for the cow that aborted, the animals in the experimental group maintained a persistant uterine motility but showed some degree of reduction in activity by the end of the experimental period. Following the abortion, the uterine contractions were as strong, rapid and distinct on the sixth postpartum day as on the first. It was evident that those cows which had the earliest calving dates maintained the most persistant and accelerated motility patterns. A comparable and consistant contraction pattern following the third day could not be established due to the introduction of several variables in the pilot experiments.

Tetanic contractions were seen in all the experimental cows but the degree varied considerably between individuals. The animals that delivered earliest exhibited the greatest number of tetanic contractions. The cow that expelled the placenta normally displayed this characteristic only by the convergence of two contractions at infrequent intervals.

In one of the animals that retained the placenta, distinct secondary, superimposed undulations were not present in as well

defined a form as they were in the other five animals in the Group. In the group as a whole, secondary undulations did not appear until the second postpartum day and were sometimes not distinct until later in the puerperium. The size of the secondary undulations varied greatly. Some were of small amplitude and short duration; recording pressures between two and four millimeters of mercury and durations of twelve seconds. Others resembled some of the smaller normal contractions. Small undulations were noted for brief periods on two of the normal tracings.

Pilot, therapeutic experiments were begun following the third recording on those cows with experimentally produced retained placenta. Antiobiotics, including penicillin, streptomycin and terramycin were employed systemically where indicated. Two cows received three million units of penieillin and two grams of dihydrostreptomycin intramuscularly on the second day of the trial when their temperatures rose above 103.2°F. The antibiotics produced no observable changes in the motility patterns of these animals (Table III - Cows 3 and 4).

The treatment employed and the motility recorded is tabulated in Table IV. The uteri of cows 1 and 2 lost their motility and their sensitivity to pitocin. As the myometrium became atonic, sacculations of fluid developed in the previously prognant uterine horns. Cows 3 and 4 maintained uterine motility throughout the experiment. The fifth cow, treated only with antibiotics and pitocin, lost the ability

UTERINE MOTILITY IN THE EXPERIMENTAL COW*- FOURTH, FIFTH AND SIXTH POSTPARTURIENT DAYS

Day 4							Day 5		Day 6						
Cow	Rect. Temp. State of Uterus	Treatment	Hours Postpartum	No. of Contr. Hour	maxmin-ye mmHg	Rect. Temp. State of Uterus	Treatment	Hours Postpartum	No. of Contr. Hour	maxmin.∀ mmHg d	Rect. Temp. State of Uterus	Treatment	Hours Postpartum	No. of Contr. Hour	waxmin.ye b, 2Hnm
1	102.6°F. Uterine horn was flaccid. Placenta liquefied.	No treatment 20 I.U. pitocin ^{#*} I. M. Recording measured 10 min. later	74•0 74•5	16.48 21.51	10 5 25 20	101.8 [°] F.	4 Salfa-Urea ^{***} bolets. PenStrep.** Stilbestrol*** All glven 24 hours previously.	100.5	15.04	4	102.2 ⁰ F. No further involution	 Sulfa-Urea bolets 25 hours previously. 20 I.U. pitocin I.M. 	126.0 127.0	00.0	0 0
2	103.6 ⁰ F. Uterine involution subnormal. Placenta retained.	No treatment	76.5	20.62	15 5	103.4 ⁰ F. Slight involution. Placenta manually removed.	4 Sulfa-Urea bolets. Terramycin I.V. All given 24 hours previously. 20 I.U. pitocin I.M.	95•5 96•5	6.00 24.00	2 10	103.4 ⁰ F. No further involution	2 Sulfa-Urea bolets 27 hours previously. Terranycin I.P. 20 I.U. pitocin I.M.	124.5 125.5	00.0 00.0	0 0
3	101.0 [°] F. Marked uterine involution.	PenStrep 24 hr. previously	80.0	27.15	30 10	103.8 ⁰ F. Marked involution.	3 Sulfa-Urea bolets. PenStrep. 22 hrs. earlier 25 I.U. pitocin I.M.	105.0 106.3	25•53 33•33	10 3 15 10	102.0 ⁰ F. Marked involution.	Terramycin I.P. 22 hours previously. 20 I.U. pitocin I.M.	128.0 129.0 129.5	32.61 41.96 30.46	5
4	102.0 ⁰ F. Involution normal. Placenta removed on 3rd day.	No treatment 20 I.U. pitocin I.M.	76.0 77.0	16.13 18.35	30 5 35 5	102.0 [°] F. Progressive involution.	No further treatment 30 I. U. pitocin I.M. Strong effect seen 2	102.0 103.0 hr. 1	16.35 37.95 ater.	10 5 30 10	102.0 ⁰ F. Marked involution.	No further treatment	125.0	****	
5	102.0 ⁰ F. Tip of horn flaccid. Other parts involuting. Placenta ret.	PenStrep. 24 hr. previously 20 I. U. pitocin I.M.	78.0 79.0	≈≈≈∎ 24•00	25	103.0 ⁰ F. Placenta liquefied. No further involution.	PenStrep. 24 hrs. previously.	100.5	****		103.0 ⁰ F. No further involution.	PenStrep. 24 hr. previously. 25 I.U. pitocin I.M.	123.0 124.0	**** 6.76	

*Data concerning length of contractions is omitted because of lack of significance. **Pitocin: Supplied through the courtesy of the Parke Davis Co. **Stibestrol: "Respositol Diethylstibestrol"

Pitman Moore Co. - 50 mg. dose.

**Sulfa-Urea: Pitman Moore Co. Each bolet con-tains 220 gr. Urea, 30 grs. Sulfanilamide and 5 gr. Sulfathiazole. Intrauterine administration.

**Pen-Strep: Procaine penicillin G in Aqueous Suspension and Dihydrostreptomycin. 1

*** Motility was present but a comparative

count was impossible. ****The cow exhibited pain at regular intervals similar to a normal cow during uterine contractions. Regular contractions however, could not be demonstrated.

TABLE IV

to produce large contractions on the third day but remained sensitive to pitocin throughout the experiment. The pregnan horn of this cow developed flaccid sacculations similar to cows 1 and 2. Cow 6 received no treatment since she did not retain the placenta and proceeded through a relatively normal puerperium in regard to involution and lack of morbid uterin changes.

All of the animals responded to pitocin at some stage of the experiment. The amount of stimulation varied primarily with the dose. Twenty units produced an increase in rate and amplitude and some tendency to form tetanic contractions. The effect of this dose as dissipated ithin one to two hours, the time being impossible to gauge accurately. The thirty unit dose that was give to co 4 produced marked tetanic spasm of the myo etrium which lasted for approximately fifteen minutes. As the tetany ubsided, the contractions regained their normal rhythm, but their amplitude resembled contractions normally recorded immediately following calving. The stimulatory effects were still present three hours following administration of the drug.

III The Histological Study of the Placentome

A study of the placentomes taken from the experimental group on the first day of puerperium revealed a lack of inflammatory cells. Sections made from second and third day specimens showed progressive leucocytic infiltration, edema and proliferation of the maternal connective tissues.

Areas of degeneration were prominent. Much of the degeneration was probably caused by delay in cutting and thoroughly exposing the tissue to the fixative.

Two of the sections which showed very little degeneration exhibited a hypertrophic trophoblast in random chorionic villi. The space normally seen between the trophoblast and the cuboidal cells lining the maternal crypts was absent in

large percent of the crypts sectioned. The cells of the trophoblast were vacuolated and completely filled the cross section of the crypts except for the appearance of a few centrally located mesenchymal and endothelial cells. The maternal connective tissue surrounding the chorionic villi appeared as thin bands of tissue only seven to ten microns thick. Low-po er examination produced a picture of masses of trophoblastic cells surrounded by thin rings of maternal connective tissue.

IV Spontaneous Abnormal Puerperiums

Four spontaneous abnormal puerperiums were observed in conjunction with the normal study. One Holstein-Friesian cow calved on the two hundred thirty-ninth day of gestation with resulting retained placenta. Only one tracing was made; at eight hours following delivery. At this time, the contraction rate was fourteen and one-half contractions per hour. The contractions were weak in comparison to those of a normal cow; however, this may have been a reflection of improper balloon size. The contraction rate was higher than all but one of the rates demonstrated in the normal group for this stage of the puerperium.

Two cows that carried their calves to full term retained the placentae. Below is a tabulation of their motility records.

TABLE V

UTERINE MOTILITY IN TWO NATURALLY OCCURRING CASES OF RETAINED PLACENTA

Hours Postpartum Gestation Length Aver.Time Aver. No. Cont Hour Sex of Calf Between Amplitude Length Breed of Cow of Contr. Contr. mm. of Hg Range Range Max.-Min. (in min.) (in min.) 284 7.0-10.0 1.687.0-10.0 1.1-2.07.09 11.0 25 5 Jer. $5.5 \underbrace{4.98}_{3.5-6.4} \underbrace{1.54}_{1.1-1.7} 12.04$ 280 30 10 Arys. F 26.6 4.62 1.32 12.00 30 10

Both of these cows sho ed active uterine motility. Their lacentae were removed manually 48 hours after parturition. The Aryshire cow's motility pattern resembled that of the experimental group in that it showed equal uterine activity on the first and second days of the puerperium.

A uterine recording was made on a Jersey cow twenty-two and one-half hours following delivery. Only one very weak contraction was recorded. Three hours later, the animal developed a classical case of milk fever.

V The Effect of ulfa-Urea and Pitocin on the Normal Puerperium

Four normal postparturient cows were treated with Sulfa-Urea (Pitman Moore Co.) as soon as the normal uterine contraction pattern as established. Tabulations of their motility patterns appear in Table VI. Uterine motility following sulfa-Urea administration was not diminished below that of the untreated normal cows. The average contraction rate of eleven and one-quarter contractions per hour during the twenty-fifth postpartum hour was nearly twice the contraction rate of six and one-third contractions per hour established by the normal group.

Twenty units of pitocin produced an observable response in all four cows in this group. The contraction rates have been tabulated in Table VI. The average contraction rate of the four cows prior to the intramuscular administration of pitocin was eleven and one-third contractions per hour. Following the administration of pitocin, the average contrac tion rate rose to nearly seventeen contractions per hour. This represented an approximate fifty per cent rate increase. The motility pattern associated with this increase varied between the individual cows. A tendency to form tetanic contractions was present in all the cows in the group but only in one case was this characteristic prominent. The amplitude of the contractions rose to a level comparable to the first few hours of the puerperium. In one case (Cow 1) the amplitude of the contractions immediately prior to the

TABLE VI

THE EFFECTS OF SULFA-UREA AND PITOCIN ON THE NORMAL PUERPERIUM

h.	Cow Breed	Je	Cow 1 r. Cros	IS		Cow 2 Jer.			Cow 3 Jer.		Cow 4 Jer.			
	Hrs. Postpartum	7.0	25.5	26.7	4.0	27.0	27.5	6.0	25.0	25.7	6.5	23.0	24.0	
	Aver.Time Between Contr. Range (in min.)	3.70 2.3 1 5.2	5.46 2.6 1 7.6		$ \frac{4.25}{3.8} 1 4.8 $	6.07 1.8 12.0 9.88		$ \frac{5.02}{3.6} 1 7.3 $	7.10 4.1 11.2		$ \frac{4.43}{2.0} $ 1 7.3 13.54	3.73 1.0 1 5.8 16.08		
A	No. of Contr. Hour	16.22	10.99		14.12			11.95	8.45					
	max./min. Amp. mm. Hg	55 15	55 25		65 25	36 20		<u>30</u> 10	<u>20</u> 5		<u>55</u> 8	$\frac{10}{2}$		
	Aver. Time Between Contr.			$\frac{3.19}{1.5}$			$\frac{3.01}{1.4}$			5.82 4.6			3.20 1.8	
	Range (in min.)		7.4.5	6.4			5.6		1.	7.0			4.4	
B	No. of Contr. Hour	Contr. 18.		18.81			19.93			10.31			18.75	
	Amp. max./min.			55 10			<u>70</u> 20			35 10		5	$\frac{30}{10}$	
	Approx. duration of action.			1 ¹ / ₂ hr.			l½ hr.			2 hrs.		Sec.	1 ¹ / ₂ hr.	

A. First recording made on normal untreated cow. Second recording made 18 or more hours after the intrauterine administration of four Sulfa-Urea bolets. B. Recording measured at the peak of activity following the intramuscular administration of 20 units of pitocin. (Parke-Davis) administration of pitocin was as high as those observed during the early hours of the puerperium. In this case, the amplitude remained unchanged even though the rate was increased. A reproduction of a typical tracing made from this group is pictured in Plate IX.

PLATE IX

THE EFFECTS OF SULFA UREA AND PITOCIN

UPON THE NORMAL PUERPERIUM

6.0 hours postpartum - Normal pattern 25 hours postpartum - 4 Sulfa-Urea bolets administered 18 hours previously. Normal pattern 26 hours postpartum - 17 minutes following administration of 20 units of pitocin intramuscularly. 10 15 5 Scale: minutes

E

DISCUSSION

The uterine motility pattern of the normal group closely resembled the pattern described by Jordan. His studies indicated a reduction in motility in direct proportion to time but he did not make a statement as to how long puerperal contractions continued. Upon comparison with data collected during the human puerperium, the cow seemed to produce contractions over a postpartum period only one-fifth as long as the human.

Since the recorded contractions were at maximum activity in both rate and amplitude during and immediately following labor, it is assumed that these puerperal contractions were merely continuations of labor contractions. Therefore, it appears reasonable that they should have disappeared or changed into the contraction pattern normally found in the cow during the estrous cycle. It would be interesting to know the entire contraction pattern from parturition until the return of estrus but this must await better methods of recording motility. It was evident, however, that the contractions of normal puerperium stopped or at least completely lost their identity within the range of sensitivity of the recording equipment employed. The appearance of secondary, superimposed undulations and irregular changes in uterine tone were suggestive of a reorganization of uterine motility in response to a changing physiological state.

The differences noted in the degree of uterine motility found in the horns and body of the uterus were in agreement with the concepts of experimenters in human medicine (Bickers, 1942; Reynolds, 1949) who expressed the opinion that an increased motility in the upper segment of the uterus coupled ith a reduction of motility in the lower segment was necesary for normal relaxation of the cervix and spontaneous childbirth.

The effects of nursing upon the bovins uterus through the release of the oxytocic principal has probably been overemphasized from the standpoint of causing immediate powerful contractions. Jordan's studies on the cow showed that uterine motility was not appreciably affected by the nursin calf and t e data presented in this paper agreed with his findings. The cows in both this study and Jordan's were observed during the early hours of puerperium. It is conceivable that a greater nursing effect could have been demonstrated during the second or third day of the puerperium when the large uterine contractions were subsiding. Perhaps the nursing calf causes the release of oxytocin at subthreshold levels in regard to the large puerperal contractions but in enough quantity to produce an important total effect upon involution of the organ and the letdown of milk.

It should be noted in these experiments that there is not always a direct correlation between uterine motility and uterine involution. This one point may be a distinct pitfall

in using this type of measurement for the evaluation of clinical response to a treatment. There is a great need for correlation studies to show the true relationship between these two phenomena.

Spontaneous retained placenta cases appeared to differ widely in their motility patterns. Jordan's three recording ere all made within three hours following delivery and it was during this early period that he reported a lack of motility as a factor or an associated condition in these retentions. The two cases that appeared in this study showed normal or, in one case, increased motility. Recordings were not made before the fifth postparturient hour but it was doubtful that the cow that exhibited twelve strong contractions per hour, five and one-half hours after delivery, would have had a different contraction pattern three hours earlier.

The motility pattern established by; 1) the experimental group whose corpora lutea were removed, 2) the cow that delivered early in the normal group and 3) the cow that aborted during Jordan's study (1952), presented a picture of increased motility and a tendency toward tetany. Although McDonald (1954) showed that experimentally produced retained placenta could be prevented by replacement therapy with progesterone, it was still not established that the increased motility following non-infectious bovine abortion was due to a deficiency of progesterone. Clinical observations have been presented in human medicine to support progesterone's inhibition of uterine activity in late puerperium (Reynolds, 1949) and this hormone has been widely used in human cases of threatened abortion. One radical difference between the naturally occurring cases of abortion described by Jordan and the experimental abortion and early-calving produced in this study by corpus ablation was the response to oxytocin. The cow that aborted during Jordan's study exhibited a high plane of uterine activity but showed no reaction to 30 units of posterior pituitary extract. All of the animals in this study whose corpora were removed responded to pitocin despite the fact that their planes of motility were above or equal to the motility of a pitocin treated, normal cow.

Although the pilot experiments were uncontrolled and lacked sufficient numbers to be significant, they sufficed in demonstrating that de ired results may not always be produced by standard treatments. Two of the experimental cows developed irreversable atonicity of a uterine horn by the end of the six-day experimental period. One of the animals showed no rise in temperature during the seventy-two hours previous to the loss of motility. The other animal maintained a body temperature between 103.4 and 103.6 degrees Fahrenheit for the last four days of the experiment, three days before complete atonicity developed. No explanation based on significant data can be given for the resultant atony. Infection, therapeutics, manipulation and many other factors could have played a part. The lack of uterine motility made a rapid recovery from placental retention impossible. The position of the affected uterine horn, over

the brim of the pelvis, beneath the abdominal viscera, made drainage difficult. Without the strong peristaltic-like contractions to empty the horn, toxic degeneration products from the placenta could only be removed by uterine massage per rectum or by the use of suction equipment. The effects of the retention of these fluids could not be accurately measured since no facilities were available for evaluating the milk production and reproduction of the affected animals. Many practicing veterinarians consider these fluids exceedingly harmful while others believe that their effects are overemphasized. The fact remains that routine treatments directed toward the morbid postparturient bovine uterus are not based upon principles and resul s formulated from controlled studies, and in many cases may be of doubtful value.

The use of Sulfa-Urea in the pilot experiments on the cases of experimentally retained placenta was always followed by a reduction in either the rate or amplitude of the uterin contractions. The experiment concerning the effects of Sulfa-Urea on the normal puerperium was designed to test the hypothesis that Sulfa-Urea had an inhibitory effect upon uterine contractions. The data presented established that no inhibition was encountered when the drug was used during the normal puerperium. It appeared that increased uterine motility may have been accomplished but the small number of cowe used in the trial made this conclusion problematical.

Pitocin was an effective stimulant to uterine motility

except in two instances where morbid changes were present in the uterus. This indicates that the use of the drug in attempts to re-establish motility in chronic clinical cases of uterine atony may be of little or no value. A twenty-unit dose of pitocin was established as a safe, effective uterine stimulant in dairy cattle weighing between seven and eight hundred pounds. When the drug was administered intramuscularly, the duration of the action as maintained from one to two hours. The only thirty-unit dose of pitocin used was administered to a large Holstein-Friesian cow during the pilot experiments. This dose produced strong reactions accompanied by pain. It seemed doubtful that a dose higher than thirty units could have been used safely without causing excessive pain and hemorrhage.

The question that immediately arose from the persistant increased motility observed in the group with experimentally retained placentae was: what was the chemical mediator for this action or was there a mediator? The immediate hypothesis that was suggested from corpus luteum removal studies in rabbits was that low progesterone levels remove the inhibitory effect of that hormone thus allowing the myometrium to respond more readily to the circulating estrogens. An explanation of the persistance of the hi rate of contraction was more obscure. The high estrogen level in the retained placenta may have been a factor but the fact that many of the placent e degenerated early and were lost as fluid uterine discharge seemed to make this answer que tionable, though plausible. Although the true cause of non-infectious retained placenta is not known, it is probable that uterine motility is not the only factor involved and probably not the most important. It is true however, that the physical act of expelling a released fetal membrane from the uterus requires the movement of the uterine wall as well as other physical forces.

The breakdown of the attachment of the chorionic villi from the maternal crypts in the caruncles remains unexplained and will remain so until the true nature of the forces holding the fetal and maternal tissues together is completely understood. If the binding force is only the physical pressure of the uterine contents then the hypotheses of Stewart (1943), Pomayer (1919), Vinding (1955) and Jordan (1953) concerning uterine motility and the effects of fetal and uterine blood pressures are well founded. If, on the other hand, the state of the binding force depends upon a delicate balance between the invasiveness of the trophoblast and the resistance of the maternal tissue controlled by steriod activity, then other factors will have to be considered. The group in which experimentally retained placenta was produced presented a picture that pointed to the possibility of the importance of the latter concept. The histological sections exhibited structural changes that appeared to make natural separation impossible. Experimentally retained placenta could not be compared with the naturally occurring cases but it could suggest the possibility of a steroid factor in producing

the condition. A therough histological study of the normal placentome during the third stage of labor is needed. With this accomplished, a comparison of the normal placentome with those from spontaneous and experimental retained placentae could be adequately attempted.

•

SUMMARY AND CONCLUSIONS

The intrauterine balloon technique was used to study bovine uterine motility during the normal puerperium and during a six day postparturient period in cows with experimentally produced retained placenta. The effects of a sulfonamide-urea preparation and a low dosage of pitocin ere evaluated in relation to the resultant changes in a normal puerperal motility pattern. Pilot experiments were made using various therapeutic designs upon cases of experimentally produced retained placenta. Histological sections were made from the placentomes of the experimental group and xamined in an attempt to demonstrate structural deviations from normal. The following new contributions have been made:

- 1. The motility pattern of the puerperium of cows with corpora lutea removed has been established which heretofore has not been reported.
- 2. This experimental group exhibited an increased contraction rate over the normal; the rates ranging from twelve to thirty-one contractions per hour.
- 3. Tetanic contractions were demonstrated in the experimental group. Comparable motility had been demonstrated only in spontaneous abortions or in oxytocin-treated normal cows.

- 4. Persistance of contractility over a six day postparturient period was recorded in the experimental group. Studies this late in the puerperium have not previously been reported.
- 5. Secondary, superimposed undulations were recorded in all but one animal in the experimental group and in two animals in the normal group. No description of such secondary undulations during the puerperium has appeared in the literature.
- 6. Uterine motility recordings were made during three day periods of treatment on cows with experimentally retained placentae. The use of the intrauterine balloon method for evaluating clinical treatment has not been heretofore reported.
- 7. Large puerperal contractions were shown to be unrecordable by the forty-eighth hour of the puerperium.
- 8. An intrauterine bolet containing sulfanilamide, sulfathiazole and urea was shown to produce no alt ration in the normal puerperal motility pattern.
- 9. Uterine motility recordings were made in two spontaneous cases of retained placenta. Both showed activity equal to or above that displayed in the normal cow at a comparable time following parturition.

In addition to thes new contributions, the following substantiate existing data:

1. The puerperal ut rine motility pattern was found to

consist initially of large rhythmic contractions which occurred at the rate of approximately fourteen contractions per hour and at an amplitude of ten to forty millimeters of mercury. Both the rate and the amplitude decreased in direct proportion to time.

- 2. Experimentally retained placenta was produced by ablation of the corpus luteum after the two hundreth day of gestation in Holstein-Friesian cows. An abortion occurred but the majority of the animals so treated maintained their pregnancies for an average of 268 days, ten days shorter than the normal Holstein-Friesian gestation period.
- 3. Twenty units of pitocin given intramuscularly effectively increased uterine motility in all of the four normal coss treated. The degree of reactivity varied between the individual cows but the limits remained within a safe therapeutic range.

This study indicated that further investigations into the cause of non-infectious retained placenta and the cause and prevention of uterine atonicity is greatly needed. Profitable information could be obtained from studies along the following lines:

1. A histological study of the placentome during: 1) the third stage of labor in normal cows, 2) spontaneous cases of ret ined placenta and 3) experimental cases of retained placenta, could yield invaluable kno ledge concerning the true state of

of the fetal-maternal attachment.

- 2. The effectiveness of uterine stimulatory drugs in treating cases of retained placenta and uterine atonicity should be evaluated.
- 3. A long-term clinical survey of the motility patterns found in spontaneous cases of retained placenta and endometritis would be of particular help to the practicing veterinarian.
- 4. A motility study of the effect of prepartum corpus luteum replacement with progesterone would clarify the function of progesterone in normal puerperal uterine motility.

BIBLIOGRAPHY

- Adair, Fred L. and Davis, dward (1934). A Study of Human Uterine Motility. <u>Amer. J. of Obst. and Gynecol.</u>, 27: 383-394.
- Bickers, William (1942). Puerperal Uterine Contractions. Amer. J. of Obst. and Gynecol., 44:581-584.
- Boyd, V. L. and Sellers, A. F. (1948). Some Observations on Postparturient Cows in Four Separate Herds as Related to Expulsion of Their Fetal Membranes. <u>Cornell Vet.</u>, 38:263-266.
- Buch, N. C., Tyler, W. J. and Casida, L. E. (1955). Postpartum Estrus and Involution of the Uterus in an Experimental Herd of Holstein-Friesian Cows. J. Dairy Science, 38:73-79.
- Coid, C. R. and *[cDiarmid, A. (1954]*. Some Observations on the Retention of the Fetal *[embranes in Dairy Cattle* After Their First Pregnancy. Vet. <u>Rec.</u>, 66:350-351.
- Csapo, Arpad and Goodall, Marcus (1954). citability, Length Tension Relation and Kinetics of Uterine Muscle Contraction in Relation to Hormonal Status. J. Physiol., 126:384-395.
- Cupps, P. T.and Asdell, S. A. (1944). Changes in the Physiology and Pharmacology of the Uterine Muscle of the Cow in Relation to the Estrus Cycle. J. Anim. Sci., 3:351-359.
- Evans, Everett I. and Miller, Fred M. (1936). Proceedings, Amer. J. of Physiol., 116:44.
- incher, M. G. (1941). Retained Placenta. J. Amer. Vet. Med. Assn., 99:395.
- Fitzpatrick, R. J. (1954). The Reactivity of the Ruminant Uterus to Oxytocin and Vasopressin. <u>Proceedings, J.</u> Physiol., 124:58.
- Foley, Richard C. and Reece, Ralph (1953). Histological Studies of the Bovine Uterus, Placenta and Corpus Luteum. Bull. Mass. Agri. Exp. Station, No. 468.

- Gardiner, Sprague and Bradbury, James T. (1940). Responses of the Human Post-Partum Uterus to Posterior Pituitary Extracts. Amer. J. of Obst. and Gynecol., 39:1-10.
- Gordon, Israel (1949). The Origin of Placental Trophoblast and the Function of Placental Gonadotrophin. Lancet, 256:807-813.
- Greenberg, Emanuel M. (1946). The Fourth Stage of Labor. Amer. J. of Obst. and Gynecol., 52:746-755.
- Hammond, John (1927). The Physiology of Reproduction in the Cow, University Press, Cambridge, London.
- Hatch, Ray D. (1941). Anatomic Changes in the Bovine Uterus During Pregn ncy. Amer. J. of Vet. Res., 2:211-216.
- Hayes, R. L. and VanDemark, M. L. (1953). Spontaneous Motility of the Bovine Uterus. <u>Amer. J. Physiol.</u>, 172: 553-556.
- Jafar, S.M., Chapman, A. B., and Casida, L. E. (1950). Caus s of Variation in Length of Gestation in Dairy Cattle. J. Anim. Sci., 9:593-601.
- Jordan, W. J. (1952). The Puerperium of the Cow; A Study of Uterine otility. J. Comp. Path., 62:54-68.
- Kennedy, A. J. (1947). Retention of the Placenta in the Bovine. <u>Vet. Rec.</u>, 59:519-523.
- Kurzrok, R., Miesbader, H., Mulinos, M. G. and Watson, B. (1937). The Action of Pituitrin, Estradiol and Progesterone on the Human Uterus in Vivo. <u>Endocrinol.</u> 21:335-342.
- 'oore, G. R. (1947). The Blood Picture in Cases of Retained Fetal Membranes in Cattle. J. Amer. Vet. Med. As n., 109:39-45.
- cDonald, Leslie E. (1952). Vaginal Approach for Removal of the Corpus Luteum. J. Amer. Vet. Med. Assn., 13:128-129.
- McDonald, Leslie E., cNutt, S. H. and Nichols, R. E. (1954). Retained Placenta - Experimental Production and Prevention. <u>Amer. J. Vet. Res.</u>, 15:22-24.
- Falmer, C. C. (1932). Clinical tudies on Retained lacenta in the Cow. J. Amer. Vet. Med. Assn., 33:59-68.
- Pomayer, C. (1908). Zuruckhalten der Nachgeburt beim Rind, Richard Schoetz, Berlin: Cited from <u>The Diseases of the</u> <u>Genital Organs in Domestic Animals</u>, W. L. Williams. <u>thel illi</u> <u>Pli pton</u>, <u>Wore ster</u>, ass., 3rd d. (1943), p.555.

- Pomayer, C. (1919). Zuruckhalten der Nachgeburt beim Rind, Berlin: Cited from <u>The Physiology of Reproduction in</u> <u>the Cow</u>. John Hammond, Cambridge University Press, London (1927), p.153.
- Ranney, Brooks and Yankton, S. D. (1956). Relative Atony of Myometrium Underlying the Placental Site Secondary to High Cornual Implantation - A Major Cause of Retained Placenta. <u>Amer. J. of</u> Obst. and Gynecol., 71:1049-1061.
- Reynolds, S. R. M. (1949). <u>Physiology</u> of the Uterus, 2nd ed., Paul B. Hoeber Inc., New York.
- Rowsan, L. E. (1955). The Movement of Radio-Opaque Material in the Bovine Uterine Tract. Brit. Vet. J., 111:334-324.
- Schatz, F. (1872). <u>Arch. of Gynak.</u>, 3:58. Cited from Wilson, Leo (1942). The Contractions of the Human Uterus During Pregnancy and Labor. <u>Amer. J. of Obst. and Gynecol.</u>, 43:955-964.
- Stewart, S. L. (1943). Retained Afterbirth in Dairy Cattle. J. Amer. Vet. Med. Assn., 103:283-285.
- VanDemark, N. L. and Hays, R. L. (1951). The Effect of Oxytocin, Adrenalin, Breeding Technique and Milking on Uterine Motility in the Cow. J. Anim. Sci., 10:1083.
- Vinding, J. (1955). Rentic secundinarum bovis. Danske Dyralaegefor. Medlemsbl., 38:23-26.
- Weeth, H. J. and Herman, H. A. (1952). A Histological and Histochemical Study of the Bovine Oviducts, Uterus and Placenta. <u>Res. Bull. Mo. Agric. Exp. Station.</u>, No. 501:54.
- Williams, W. L. (1943). The Diseases of the Genital Organs of the Domestic Animals, Ethel Williams Plimpton. Worcester, Mass., 3rd ed.
- Wimsatt, William (1953). Observations on the Morphogenesis, Cytochemistry and Significance of the Binucleate Giant Cells of the Placenta of Ruminants. <u>Amer. J. Anat.</u>, 89:233-281.

VITA

John Howard Venable

Candidate for the Degree of

Master of Science

Thesis: POSTPARTURIENT BOVINE UTERINE MOTILITY FOLLOWING EXPERIMENTALLY PRODUCED RETAINED PLACENTA

Major Field: Physiology

Biography:

Born: October 16, 1929, at Oklahoma City, Oklahoma
Undergraduate Study: Doctor of Veterinary Medicine
Degree from Oklahoma A. and M. College, May, 1953.
Graduate Study: Oklahoma Agricultural and Mechanical
College, 1954-1956.
Professional Experience: Private practice of Veterinary Medicine, Norman, Oklahoma, 1953-1954,
Springfield, Missouri, 1954; Instructor in
Veterinary Anatomy, Oklahoma Agricultural and
Mechanical College, 1954-1956.

Honorary and Professional Societies: Phi Sigma; American Veterinary Medical Association; American Association of Veterinary Anatomists; Animal Disease Research Workers in Southern States.