AI beef management with prostaglandin F□2a controlled estrus
by Paul Wilson Lambert

A thesis submitted in partial fulfillment of the requirements for the degree of MASTER OE SCIENCE in Animal Science
Montana State University

Abstract:
Breeding studies were conducted utilizing PGF2a as an estrus synchronizing agent in beef cattle. Seven groups of cattle were utilized which consisted of (Cl, Fall 1974 bred heifers, n=92), (G2, Fall 1974 bred early calving cows, n=148), (G3, Fall 1974 bred late calving cows, n=85), (G4, Spring 1975 bred 14 mo. neifers, n=87), (G5, Spring 1975 bred 20 mo. heifers, n=324). Cattle in groups I, 4 and 5 were straight and crossbred virgin heifers. Cattle in groups 2, 3, 6 and 7 consisted of straight and crossbred lactating cows.

Cattle within each group were randomly assigned to a PGF2a system or a conventional system. Al was used for 30 days Cl, 28 days G2, 22 days G3 and 25 days for G4, G5, G6 and G7. In all groups a 20 day natural breeding season followed. Cattle in the PGF2a system were observed for estrus and bred from day -% to 4 at which time the remaining cattle were injected IM with 33.5 mg PGF2a THAM-salt. At 72 hr (groups 1, 2 and 3) or 80 hr (groups 4, 5, 6 and 7) post-injection, all PGF2a treated cows not observed in estrus were inseminated. At the time of the nonestrus breeding in groups 4, 5, 6 and 7 half of the cattle that fell into this catagorie were reinjected with 33.5 mg of PGF2a immediately after insemination. Conception dates were confirmed based on actual calving dates. The total pregnancy rate (combined analysis, groups I through 7) for the PGF2a system was significantly higher (78 vs 72%, P=0185) than in the conventional system. The total Al pregnancy rate (combined analysis) for the PGF2a system was significantly higher (47 vs 39%, P=.0016) than in the conventional system. There were no significant differences between systems (combined analysis) for Al 1st service pregnancy rate of Al 1st service conception rate when bred to an observed estrus. The number of cows conceiving the first 10 days of the Al season (combined analysis) was greater (P<.001) in the PGF2a system than in the conventional breeding system. This resulted in the average day of conception being 5 days earlier in the PGF2a breeding system (day 17) compared to the conventional system (day 22). There was a trend for decreased estrus response and AI 1st service pregnancy rate for PGF2a treated cattle that were between 69 and 80 days postpartum on the day PGF2a was administered.

The cattle receiving the second injection of PGF2a at the 80 hr nones trus breeding revealed no significant differences in total pregnancy rate, total AI pregnancy rate or AI 1st service pregnancy rate when compared to controls.

STATEMENT OF PERMISSION TO COPY

In presenting this thesis in partial fulfillment of the requirements for an advanced degree at Montana State University, I agree that the Library shall make it freely available for inspection. I further agree that permission for extensive copying of this thesis for scholarly purposes may be granted by my major professor, or, in his absence, by the Director of Libraries. It is understood that any copying or publication in this thesis for financial gain shall not be allowed without my written permission.

Signature Paul W. Lambert Jr

Date 6-14-77

AI BEEF MANAGEMENT WITH PROSTAGLANDIN $F_{2\alpha}$ CONTROLLED ESTRUS

by

PAUL WILSON LAMBERT JR.

A thesis submitted in partial fulfillment
of the requirements for the degree

of

MASTER OF SCIENCE

in

Animal Science

Approved:

Edward L. Moody
Chairperson, Graduate Committee

David K. Han
Co-chairperson, Graduate Committee

J. L. Van Horn
Head, Major Department

Harry L Parsons
Graduate Dean

MONTANA STATE UNIVERSITY
Bozeman, Montana

June, 1977

ACKNOWLEDGEMENTS

I wish to express my sincere appreciation to Dr. E. L. Moody and Mr. D. K. Han for their advice, assitance and guidance throughout my graduate program. Appreciation is also expressed to Drs. P. Burfening, O. Thomas and C. Greer, the other members of my graduate committee.

A special word of thanks is extended to Mr. William M. Greene for his help in collecting the data for and consultation in preparing this manuscript in addition to his just being a good friend.

I would also like to thank my fellow graduate students who gave assistance at various times during these studies, especially Vern LaVoie, David Griswold, Jim Strickland, John Williams, John Pickett, Steve Prier, Robert Friedrich and Mike MacNeil.

A special word of appreciation is due to Mr. Don Smith and the staff of the Montana State Prison Ranch, Deer Lodge, Montana, for assisting me in collecting the data and for the use of cattle and facilities.

I would also like to thank Drs. Lauderdale and Pike, Upjohn Company, Kalamazoo, Michigan, for supplying the prostaglandin $F_{2\alpha}$ and American Breeders Service, DeForest, Wisconsin, for supplying the semen used in this study.

The support and encouragement of my wife Marilyn and my son Paul during this work is greatly appreciated as is the assistance and encouragement of my wife's family, Don and Betty Keesler.

Furthermore, my sincere gratitude is expressed to Mrs. Frankie Larson for typing this manuscript.

TABLE OF CONTENTS

INDEX TO TABLES

INDEX TO FIGURES

INDEX TO APPENDIX FIGURES

Figure | Page

ABSTRACT

Breeding studies were conducted utilizing $PGF_{2\alpha}$ as an estrus synchronizing agent in beef cattle. Seven groups of cattle were utilized which consisted of (G1, Fall 1974 bred heifers, n=92), (G2, Fall 1974 bred early calving cows, n=148), (G3, Fall 1974 bred late calving cows, n=85), (G4, Spring 1975 bred 14 mo. neifers, n=87), (G5, Spring 1975 bred 20 mo. heifers, n=324). Cattle in groups 1, 4 and 5 were straight and crossbred virgin heifers. Cattle in groups 2, 3, 6 and 7 consisted of straight and crossbred lactating cows. Cattle within each group were randomly assigned to a $PGF_{2\alpha}$ system or a conventional system. AI was used for 30 days G1, 28 days G2, 22 days G3 and 25 days for G4, G5, G6 and G7. In all groups a 20 day natural breeding season followed. Cattle in the $PGF_{2\alpha}$ system were observed for estrus and bred from day -½ to 4 at which time the remaining cattle were injected IM with 33.5 mg $PGF_{2\alpha}$THAM-salt. At 72 hr (groups 1, 2 and 3) or 80 hr (groups 4, 5, 6 and 7) post-injection, all $PGF_{2\alpha}$ treated cows not observed in estrus were inseminated. At the time of the nonestrus breeding in groups 4, 5, 6 and 7 half of the cattle that fell into this catagorie were reinjected with 33.5 mg of $PGF_{2\alpha}$ immediately after insemination. Conception dates were confirmed based on actual calving dates. The total pregnancy rate (combined analysis, groups 1 through 7) for the $PGF_{2\alpha}$ system was significantly higher (78 vs 72%, P=0185) than in the conventional system. The total AI pregnancy rate (combined analysis) for the $PGF_{2\alpha}$ system was significantly higher (47 vs 39%, P=.0016) than in the conventional system. There were no significant differences between systems (combined analysis) for AI 1st service pregnancy rate of AI 1st service conception rate when bred to an observed estrus. The number of cows conceiving the first 10 days of the AI season (combined analysis) was greater ($P<.001$) in the $PGF_{2\alpha}$ system than in the conventional breeding system. This resulted in the average day of conception being 5 days earlier in the $PGF_{2\alpha}$ breeding system (day 17) compared to the conventional system (day 22). There was a trend for decreased estrus response and AI 1st service pregnancy rate for $PGF_{2\alpha}$ treated cattle that were between 69 and 80 days postpartum on the day $PGF_{2\alpha}$ was administered. The cattle receiving the second injection of $PGF_{2\alpha}$ at the 80 hr non-estrus breeding revealed no significant differences in total pregnancy rate, total AI pregnancy rate or AI 1st service pregnancy rate when compared to controls.

CHAPTER 1

INTRODUCTION

The ever increasing pressure of the cost-price squeeze, on the nation's beef producers, emphasizes the need for more efficient production in the beef cattle industry. To deal with this cost-price squeeze, the progressive beef producer has turned to sophisticated management systems involving artificial insemination, to increase the pounds of salable product. One economically important aspect of artificial insemination in Montana, is the labor it requires for estrus detection. With the perfection of an estrous synchronization system that minimizes or eliminates estrus detection, the labor requirement could be greatly reduced during the breeding, as well as the calving season.

Extensive data demonstrates prostaglandin $F_{2\alpha}$ to be luteolylic in the cow (Lauderdale, 1972; Liehr et al., 1972; Rowson et al., 1972; Inskeep, 1973; Lamond et al., 1973; Stellflug et al., 1975; LaVoie et al., 1975). Extensive research has shown that prostaglandin $F_{2\alpha}$ can provide an effective method of controlling estrus in the cow and that fertility of the synchronized estrus is comparable to control cows (Inskeep, 1973; Lauderdale et al., 1974; Welch et al., 1975; Lambert et al., 1975; Lambert et al., 1976; Manns et al., 1976; Burfening et al., 1976).

The purpose of this study was to field test the effectiveness of a prostaglandin $F_{2\alpha}$ controlled estrus system under Montana range beef production conditions where no more than two handlings (including insemination) of each cow are required.

CHAPTER 2

LITERATURE REVIEW

Endocrine Events of a Normal Estrous Cycle

A Schematic illustration of the interrelationships between the hypothalamus, pituitary and ovary and the possible regulatory influence of the uterus are depicted in figure 1.

The release of gonadotropin releasing hormone (Gn-RH) from the hypothalamus will be used as the initiating event in the model estrous cycle. Kaltenback et al. (1974) demonstrated that Gn-RH acts to promote the secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary. The exact role of FSH is not precisely understood. The hypothesis of Schwartz (1974) is that FSH in combination with LH at continuously low levels enhances follicular growth and maturation. As the follicles mature they release estrogens from the theca interna cells. Austin and Short (1972) and Schwartz (1974) indicate that estrogen production from the theca interna cells is stimulated by low levels of LH and possibly FSH. Estrogen acts on target cells in the uterus (stimulating growth and proliferation) and also on the hypothalamo-pituitary axis (Caldwell, 1970). The increasing levels of estrogen during the follicular phase of the cycle exerts an effect on the hypothalamo-pituitary axis which results in the release of peak levels of LH, FSH and prolactin during estrus (Niswender et al., 1974). It is suggested that the increased secretion of LH and FSH may be due to increased release of Gn-RH from the

hypothalamus or to increased sensitivity of LH and FSH secreting cells within the adenohypophysis to Gn-RH (Niswender et al., 1974). LH is thought to promote final maturation of the follicle and eventual ovulation followed by formation of a corpus luteum (CL). Strott et al. (1969) indicated that LH may act to stimulate the secretion of progesterone from the corpus luteum in some species. This is thought to be accomplished by the transformation of granulosa cells from the ruptured follicle into luteal cells which secrete progesterone. Harris and Campbell (1966) (as reviewed by Caldwell, 1970) indicate that LH is luteotropic in most species and prolactin is accepted as a co-hormone of the luteotropic complex in the rat. Hansel et al. (1973) presented conclusive evidence that LH is luteotropic in the cow. As the corpus luteum develops, progesterone secretion increases until maximum output at about day 12 of the bovine estrous cycle. This output remains fairly constant until day 16 of the cycle when corpus luteum regression occurs if conception has not occurred (Hansel et al., 1973). If the previous sequence of events does not result in conception, the next ovarian cycle will begin. Investigations dealing with control of ovarian periodicity have revealed that in several species, including the cow, the uterus exerts control over the CL by the release of a uterine luteolytic factor (ULF) (Loeb, 1923, Hecter et al., 1940; Wiltbank and Casida, 1956; and LaVoie et al., 1975). Special treatment of this area will follow in the next section.

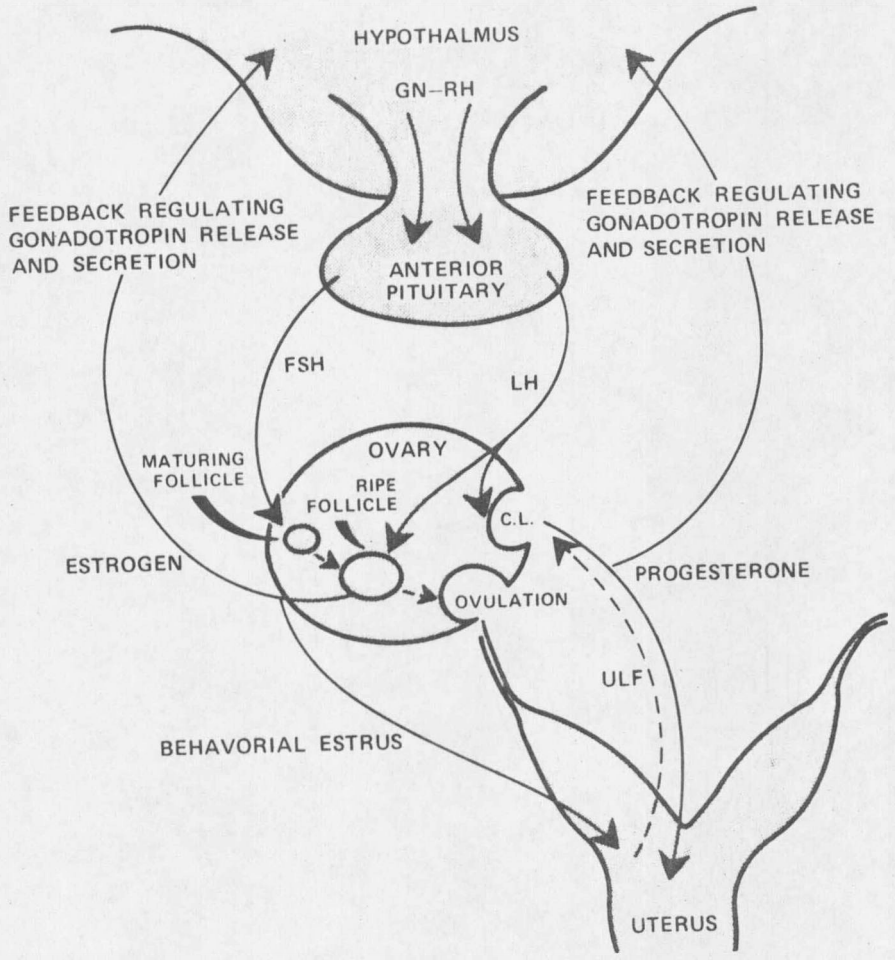

Figure 1. Principle endocrine pathways involved in the control of ovarian function.

Uterine Luteolytic Factor

Melampy and Anderson (1968) indicated that the uterus has an important role with regard to the control of the luteal mechanism via initiation of luteolysis during the later stages of the estrous cycle.

Though many of the questions relating to ovarian periodicity have been answered, many still remain unanswered. The following literature indicates that the uterus and particularly its endometrial layer secretes a luteolytic substance prior to the onset of corpus luteum regression.

Many studies have been performed involving removal, transplantation, partial destruction and denervation, in an attempt to determine the origin and isolate the compound(s) which exert control over ovarian periodic activity.

Removing the uterus. It was first reported by Loeb (1923) that hysterectomy prolonged the functional life span of the corpora lutea in the guinea pig for 60 to 80 days. The principle function of the corpus luteum in unmated animals is to control the length of the diestrous phase of the estrous cycle (Melampy and Anderson, 1968). It was also observed by Loeb (1923) that subsequent maturation of follicles and ovulation is not effected by uterine removal in very young animals. In addition, Loeb found that a small portion of uterine tissue remaining intact will cause corpus luteum regression; however, the resulting cycle length is usually longer than normal. Since Loeb's discovery, a luteolytic factor thought to be released from the uterus (ULF) has

been sought. Hechter (1940) advanced the idea that the uterus may produce a compound(s) which causes the corpora lutea to regress and in its absence the corporal lutea will be maintained.

Wiltbank and Casida (1956) demonstrated that complete removal of the uterus in the ewe or cow resulted in maintenance of the corpus luteum. Corpora lutea were maintained for as long as 100 days in the ewe and 154 days in the cow. Removal of approximately half of the uterus in the ewe caused no delay in the return to estrus. Nearly complete removal of the uterus in the cow caused delay in the return to estrus.

In 1961, duMesnil du Buisson partially hysterectomized pigs and found the uterus to have local lutolytic properties where each uterine horn of the bicornuate system controls only the CL of its adjacent ovary.

Barley et al. (1956) working with pseudopregnant rats, observed a localized effect of unilateral hysterectomy on the corpus luteum. In addition, he found that an intact uterine horn on one side of the uterus could appreciably shorten the life expectancy of luteal activity on the contralateral ovary. The results from these experiments suggest that the luteolytic factor from the uterus has access to systemic circulation and that the compound(s) is effective even when only a small portion of uterus remains intact.

Partial hysterectomy in the unmated guinea pig, heifer, sow and ewe ultimately results in luteal regression and the continuation of estrous cycles (Butcher et al., 1962; Anderson et al., 1961; Anderson, 1962; Rowson and Moor, 1964). In these species the amount of intact uterine tissue (endometrium) tends to dictate the functional life span of the CL.

Ginther (1967) reported that in heifers with the retained horn adjacent to the corpus luteum the functional life span of the CL was shorter than if the retained horn was opposite to the corpus luteum. Both cases resulted in luteolysis. This evidence suggests that ULF is effective more rapidly on a local basis, but can be effective systemically.

Anderson et al. (1963) found that removing the uterus at days 5, 10, 14 and in some cases on day 16 resulted in continual development (when hysterectomized at day 5) and prolonged maintenance of the CL in the pig. Hysterectomy on day 18 did not result in prolonged maintenance, indicating that if there is a luteolysin released from the uterus, it has been released prior to day 18 of the cycle.

When freeze-dried endometrium from sheep in days 14 or 15 of their cycle was injected intraperitoneally into hysterectomized hamsters on days 9 and 10 of pseudopregnancy, a significant reduction of the corpora lutea life span was recorded in nine of 16 animals (Caldwell et al., 1969). Extracts prepared from other days in the

cycle had little effect on the corpus luteum. This evidence indicates that the endometrium contains an active luteolytic substance during the later part of the sheep estrous cycle.

Transplantation of the uterus. In 1966, duMesnil du Buisson (reviewed by Melampy and Anderson, 1968) found sows to have estrous cycles after uterine tissue autotransplants to the body wall but not when similar transplants were made to the small intestine. This indicated that the luteolytic factor from the uterine tissue was inactivated when subjected to the portal circulation of the small intestine which passes through the liver.

It was demonstrated that homologous transplantation of uterine endometrial tissue to the cheek pouch of the hamster would partially reverse the effect of hysterectomy (Caldwell et al., 1967). Mazor and Wright (1968) varified that the effects of hysterectomy on pseudopregnant hamsters can be reversed by homologous uterine transplantation to the cheek pouch. Pseudopregnancy was shortened by more than six days following transplantation of seven-day pseudopregnant uterine horns. No decrease in pseudopregnancy was observed when uterine extracts were prepared from pregnant hamster horns which indicates that pregnancy inactivates ULF.

Evidence for ULF in the cow was demonstrated by Williams et al. (1967). They injected acetone dried powder preparations of late luteal and early estrual bovine uteri intraperitioneally into pseudopregnant rabbits. The prepartations induced regression of corpora lutea,

development of follicles and a depression of acetate incorporation into progesterone.

Partial destruction of the uterus. Anderson et al. (1961) removed the left horn from the uterine body to the tubo-uterine junction on day 11 or 12 of the pigs estrous cycle. The right horn and body were infused with either (a) 10% tannic acid: (b) 12.5% phenol: (c) Bouin's solution; or (d) 10% silver nitrate. The animals were sacrificed about 48 days after the estrus before treatment. Estrus behavior was not observed during this period. Marked corpora lutea were present at the termination of the experiment which indicate that irritants and corrosives alter uterine function in such a way as to bring about a persistence of corpora lutea.

The life span of guinea pig corpora lutea was extended after injection of an irritant or a corrosive into the lumen of the uterine horns. The greatest prolongation was observed in animals with the most endometrial destruction (Butcher et al., 1962).

Denervation of the uterus. In a review by Melampy and Anderson (1968) it is indicated that denervation of the uterus has no effect on luteal regression and follicular development in the sow.

Luteolysis

Corpus luteum regression. Hansel et al. (1973) defines regression of the bovine corpus luteum as a decrease in cytoplasmic granulation, rounding of the cell outline and peripheral vacuolation of the large

luteal cells. These changes are rapidly followed by condensation of the cytoplasm, which stains darkly and takes on a stellate outline. The first nuclear change noted is a loss of prominent nucleoli followed by shrinkage. Connective tissue becomes more prominent along with thickening of the walls of the arteries and by day 2 of the cycle the lumina of many arterioles are obliterated. This definition of CL regression (luteolysis) will be utilized for purposes of discussion in this thesis.

Donaldson and Hansel (1965) found in the cow that between days 4 and 7 of the estrous cycle the corpus luteum increased in size (1.3 to 4.6 g) and progesterone content (38.0 to 145.0 ug), but the progesterone concentration did not vary (30.0 to 31.7 ug/g of tissue).

It was shown that the principal progestin in the CL and ovarian venous blood diminishes rapidly towards the end of the cycle from maximum levels observed during mid-cycle (Gomes and Erb, 1965).

In 1964, Kenney (as reviewed by Hansel, 1973) stated that progesterone synthesis slows and stops as a result of an "uncoupling" of the steroid synthetic mechanism from the metabolic systems which supply it with energy and precursors. It was also suggested that corpus luteum involution results from a reduction in its blood supply brought about by three types of sclerotic arterial changes which become the basis of a working hypothesis for the mechanism of luteolysis.

The decline in progesterone synthesis has been related to an

increase in the number of lysosomes in the luteal cells. In sheep, the luteolytic mechanism(s) act directly on the lysosomes to increase their fragility and initiate luteal regression (Dingle et al., 1968).

Moor (1968) demonstrated that in several species including the sheep, that presence of embryos in the uterus prolongs the life span of the corpus luteum. The functional capacity of the CL is not increased as evidence by the level of progesterone secreted by the corpus luteum of pregnancy which is found to be similar to the maximum level secreted during the estrous cycle. The effect of embryos is first seen on days 12 to 13 of the sheep estrous cycle. It is suggested that this effect is accomplished by "protecting" the corpora lutea from the luteolytic effect of the uterus or by preventing the uterus from secreting its luteolytic agent.

Luteolytic agents. Hansel et al. (1973) summarized that LH appears to be the major luteotropic principle in all three domestic animals (cow, ewe and sow) and that there is little evidence that it can cause luteolysis as it has been observed in the rabbit. Their data reveal that plasma LH levels do not decline prior to the decline in plasma progesterone. They suggest that the response of the corpus luteum to LH is "switched off" by the luteolytic mechanisms(s).

Malven and Hansel (1964) found that ten daily injections of crude or urea-incubated aqueous extracts of bovine hypophyiseal tissue did not decrease the progesterone content of the corpora lutea which

persist following hysterectomy. In fact administration of the crude extracts increased the total weight and progesterone content of the corpora lutea. The urea incubated extracts inactivate luteinizing hormone in an attempt to observe the effect of FSH and prolactin on luteal function. No luteolytic effects by FSH and prolactin were observed.

Lynn et al. (1965) used 41 virgin heifers to study the effects of in vivo treatment with FSH, oxytocin, HCG and bovine prolactin upon the ability of the CL to synthesize progesterone. No significant effects of oxytocin or prolactin along were observed. FSH treatment produced a significant depression of progesterone synthesis by luteal slices in vitro. HCG in vivo produced a drop in initial progesterone concentration while in vitro it enhances progesterone production ($P<.01$).

Brunner et al. (1969) made a study on the luteolytic effects of various pituitary and ovarian hormones. Intact cycling heifers were injected with estradiol (n=5, on days 10 through 14 of their estrous cycle) or ACTH (n=6, on days 2 through 8 of their estrous cycle). Forty-three normal cycling heifers were hysterectomized on day 10 of of the cycle (day 0=day of estrus) and their corpora lutea were marked with a charcoal suspension. Following hysterectomy (21 days), when the CL's were 30 days old, each heifer was placed on one of the following treatments: (1) oxytocin, 0.33 USP units/kg/day subcutaneously

for 30 days; (3) equine luteinizing hormone 20 mg/day subcutaneously of 15 days; (4) estradiol 17_B 5 mg/day intramuscularly in peanut oil for six days; (5) estradiol-17_B, 5 mg/day intramuscularly for 15 days; (6) relaxin, 6000 GPU/day intramuscularly for 15 days; (7) control, six days; (8) control, 15 days; (9) control, 30 days. An additional group of ten heifers were hysterectomized on day 10 of the cycle. Ten days after hysterectomy, five of these heifers were injected daily with ACTH for six days (two at a rate of 100 units/day and three at 200 units/day). The remaining five heifers served as controls. Oxytocin injections had no luteolytic effects. Equine luteinizing hormone increased progesterone concentration, total progesterone and total progestins. Estradiol significantly depressed total progesterone. Estradiol injected into intact heifers on either days 5 through 14, or 10 through 14 of their cycle caused complete luteal regression. Relaxin injected into hysterectomized heifers had no luteolytic effect. Adrenocorticotropin injected on days 2 through 8 of their cycle significantly decreased corpus luteum weight in intact heifers but was ineffective when injected into hysterectomized heifers.

Wagner et al. (1971) found that after injecting five cyclic heifers with 5 mg flumethasone IM on days 1 through 8 of the estrous cycle, CL weight (g), progesterone content (ug/g) and total ug of progesterone were 6.3, 47.5 and 302 for the treated and 5.6, 67.4 and 378 for the control CL's (n=5), respectively. They also found that

plasma progesterone was elevated above control levels during the first 5 days of treatment with ACTH (100 units/day) beginning on day 1, however, continued ACTH treatment (100 units/day on days 6-8 inclusive) caused plasma progesterone to fall below that found in control animals.

Greenstein (1958) administered estradiol subcutaneously to reproductively normal cycling cows at several dose levels and at various stages of estrous cycle, in an attempt to modify reproductive processes. His findings indicate that suppression of follicular development and early regression of the bovine corpus luteum resulted from daily treatment with 1-2 mg of estradiol from day 2 to day 12 of the cycle.

Wiltbank (1961) conducted 3 trials in which various forms and levels of estrogen were injected into cycling beef heifers. Single injections of 50, 25, 20, 10 and 5 mg of estradiol valerate; or of 100, 50 and 25 mg of estrone; or of 25 mg of a natural estrogenic product caused early regression of the corpus luteum in more than 50% of the heifers injected. This data supports previous data demonstrating that single intramuscular injections of estradiol valerate or estrone would cause early CL regression.

Brunner et al. (1969) found essentially complete luteal regression in intact heifers by a dose of estradiol that produced only a small, nonsignificant decline in CL weights and a relatively small decrease in total progesterone contents in corpora lutea of hysterectomized animals. These findings indicate that estradiol induced luteolysis requires the presence of the uterus.

Hawk and Bolt (1970) injected parous ewes intramuscularly with 250 or 750 ug of estradiol-17_B per day for 2 successive days, beginning on alternate days of the estrous cycle from days 1 through 11 (estrous= day 0). There was no luteolytic effect with either the 250 or 750 ug dose of estradiol on days 1 and 2, 3 and 4, or 5 and 6. However, the 750 ug dose on days 9 and 10 reduced CL weight significantly by day 14 while either the 250 or 750 ug dose on days 11 and 12 reduced CL weights significantly by day 15. Their data indicate that injections of estradiol during the last week of the estrous cycle reduces CL weight. Hansel et al. (1973) indicated that the luteolytic effects of exogenous estrogens in the cow and the ewe are of particular interest, especially when considering the fact that plasma estrogens appear to rise in both species before luteal regression is initiated.

Harms and Malven (1969) found that estrous cycle length in heifers was reduced significatnly following progesterone (100 mg daily) injected on days 1 to 3 (13.6 day cycle length) or on days 2 to 6 (16.5 day cycle length). The progesterone treatment reduced CL weight significantly when given early in the cycle.

Woody and Ginther (1968) studied the effects of exogenous progesterone on CL weight and life span in intact, or ipsilateral and contralaterally hysterectomized heifers. There was a greater reduction in estrous cycle length when progesterone injections were started on the day of estrus than when started two days after. When measured at

day 15, CL weight was not significantly affected by progesterone treatment (100 mg per day, days 1 through 10), or uterine condition (intact, ipsilateral or contralateral). Progesterone treatment on days 1 through 10 reduced the average estrous cycle length in intact heifers. When the heifers were ipsilaterally hysterectomized and given a similar progesterone treatment early in the subsequent estrous cycle, the cycle length was reduced, but it was not reduced in contralaterally hysterectomized heifers given progesterone. This data indicates that if progesterone is administered during the early part of the estrous cycle and if the uterine horn ipsilateral to the CL is present, the cycle length will be reduced. It was postulated that progesterone given early in the cycle may act by inhibiting the relatively small rise in plasma LH found to occur on day 3 to 4 of the cycle (Wilks and Hansel, 1971) which may be a stimulus that causes maximum CL development and progesterone secretion after day 4.

Woody et al. (1967) injected intact ewes with 25 mg of progesterone per day for the first 6 days of the estrous cycle. The average length of the estrous cycle was reduced from 16.5 days in control ewes to 12.7 days in treated ewes.

It appears that exogenous progesterone decreases the length of the cycle in cattle and sheep. The data presented so far, suggest that progesterone does not cause CL regression, however it may be acting by inhibiting the critical amounts of gonadatropins necessary to

stimulate luteal development and maintenance. It was discussed that progesterone requires uterine tissue to be present. This is supported by the fact that progesterone is less effective in hysterectomized than in intact ewes.

Hansel and Wagner (1960) infused 2 to 5 ml of raw semen, or the sediment obtained by centrifuging raw semen and preputial fluids into the uterus of heifers at estrus. A large proportion of the heifers returned to estrus between the sixth and thirteenth days of the subsequent cycle.

It was first suggested by Babcock (1966) that prostaglandins might be luteolytic in domestic livestock. $PGF_{2\alpha}$ has been demonstrated to be luteolytic in the cow (Lauderdal, 1972), ewe (McCracken et al., 1971) sow (Diehl and Day, 1973) and the mare (Douglas and Ginther, 1972).

Is $PGF_{2\alpha}$ the ULF?

As stated by Pharris et al. (1972), for prostaglandin $F_{2\alpha}$ to be the endogenous luteolytic factor, five criteria would have to be satisfied (1) $PGF_{2\alpha}$ must be luteolytic in all species where the uterus is implicated in luteal function (2) prostaglandins must cause luteolysis when administered systemically and on a local basis (3) $PGF_{2\alpha}$ must be present in or released from the endometrium at a time consistent with uterine induced luteolysis (4) pregnancy should counteract the presence or action of $PGF_{2\alpha}$ and (5) the luteolysis induced by $PGF_{2\alpha}$ should mimic spontaneous luteolysis, biochemically, morphologically and

functionally.

1. "$PGF_{2\alpha}$ must be luteolytic in all species where the uterus is implicated in luteal function".

Pharris and Wyngarden (1969) infused prostaglandin $F_{2\alpha}$ into pseudopregnant rats for 2 days (day 5 and 6) at 1 mg/kg/day. The progestogen content of the ovaries of these animals was compared to that of animals receiving only saline. Progesterone levels were decreased, 20 dihydropogesterone concentrations were increased and a decrease in the length of pseudopregnancy to 7 days from a normal of 14 days occurred.

Pharris (1970) tested $PGF_{2\alpha}$ on pseudopregnant rabbits. Prostaglandin $F_{2\alpha}$ (5 mg/kg/day) was given on days 4 through 8 of pseudopregnancy, and the ovaries were collected on day 12. $PGF_{2\alpha}$ was 100% luteolytic in treated animals while 11 of 12 controls had normal appearing luteninized ovaries.

Batchley and Donovan (1969) studied the luteolytic effects of $PGF_{2\alpha}$ in guinea pigs (n=21) hysterectomized on day 4 or 5 of the cycle (estrus=day 1). Six of the animals were injected IP with 0.5 mg $PGF_2{}^{\alpha}$ twice daily for 7 days and 5 of these showed advanced luteal regression as compared with controls.

McCracken et al. (1970) demonstrated in two sheep bearing left ovarian autotransplants (to the vessels of the neck with vascular anastomoses) which were in the midluteal phase of the cycle that $PGF_{2\alpha}$