



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 OF SCIENCE
in Animal Science

Montana State University

© Copyright by Paul Wilson Lambert (1977)

Abstract:

Breeding studies were conducted utilizing PGF_{2a} as an estrus synchronizing agent in beef cattle. Seven groups of cattle were utilized which consisted of (C1, 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. heifers, 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_{2a} system or a conventional system. AI was used for 30 days C1, 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_{2a} system were observed for estrus and bred from day -% to 4 at which time the remaining cattle were injected IM with 33.5 mg PGF_{2a} THAM-salt. At 72 hr (groups 1, 2 and 3) or 80 hr (groups 4, 5, 6 and 7) post-injection, all PGF_{2a} 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 category were reinjected with 33.5 mg of PGF_{2a} 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_{2a} system was significantly higher (78 vs 72%, P=0.185) than in the conventional system. The total AI pregnancy rate (combined analysis) for the PGF_{2a} 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_{2a} system than in the conventional breeding system. This resulted in the average day of conception being 5 days earlier in the PGF_{2a} 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_{2a} treated cattle that were between 69 and 80 days postpartum on the day PGF_{2a} was administered.

The cattle receiving the second injection of PGF_{2a} at the 80 hr nonestrus 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_{2α} 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
ad Head, Major Department

Henry 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, assistance 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

	Page
VITA.	ii
ACKNOWLEDGMENTS	iii
INDEX TO TABLES	viii
INDEX TO FIGURES.	xi
INDEX TO APPENDIX FIGURES	xii
ABSTRACT.	xiv
CHAPTER 1	1
INTRODUCTION	1
CHAPTER 2	3
LITERATURE REVIEW.	3
Endocrine Events of a Normal Estrus Cycle.	3
Uterine Luteolytic Factor.	6
Removing the uterus	6
Transplantation of the uterus	9
Partial destruction of the uterus	10
Denervation of the uterus	10
Luteolysis	10
Corpus luteum regression.	11
Luteolytic agents	12
Is PGF ₂ α the ULF?.	18
Prostaglandins	27
A brief history	27
Basic chemistry and biosynthesis of prostaglandins.	27
The mechanism of action of PGF ₂ α	29

	Page
Postulate One (PGF _{2α} blocks the pituitary or luteotropic complex)	29
Postulate Two (PGF _{2α} stimulates the uterus to release luteolysin)	30
Postulate Three (PGF _{2α} has a direct toxic effect on the CL)	30
Postulate Four (PGF _{2α} exerts an antigonadotropic action)	31
Postulate Five (PGF _{2α} caused constriction of the utero-ovarian vein)	31
Estrus Synchronization	32
Exogenous steroid therapy	34
Synchronization with PGF _{2α}	37
CHAPTER 3	46
MATERIALS AND METHODS	46
CHAPTER 4	51
Results and Discussion of the Fall 1974 Breeding Season Based on Pregnancy Test Results	51
Summary	53
CHAPTER 5	63
Results and Discussion of the Spring and Fall 1975 Breeding Seasons based on Pregnancy Test Results	63
Summary	66
CHAPTER 6	76
Results and Discussion of the Fall 1974, Spring and Fall 1975 Breeding Seasons based on Calving Results	76
Summary	92

	Page
APPENDIX	102
LITERATURE CITED	115

INDEX TO TABLES

Table	Page
1 TOTAL PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)	55
2 TOTAL AI PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)	56
3 AI FIRST SERVICE PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)	57
4 AI FIRST SERVICE PREGNANCY RATE WHEN BRED TO AN OBSERVED ESTRUS IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)	58
5 AI FIRST SERVICE CONCEPTION RATE WHEN BRED NONESTRUS AND RECEIVED PGF2 α (ALL 1974 BREEDING)	59
6 INCIDENCE OF FIRST ESTRUS IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)	60
7 PERCENT OF BEEF CATTLE PREGNANT THE FIRST TEN DAYS OF THE AI BREEDING SEASON WITH ONE AI SERVICE IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)	61
8 THE AVERAGE DAY OF CONCEPTION IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (AI AND SUBSEQUENT NATURAL BREEDING SEASON INCLUDED) (ALL 1974 BREEDING)	62
9 TOTAL PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975 BREEDING)	68
10 TOTAL AI PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975 BREEDING)	69

Table	Page
11 AI FIRST SERVICE PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975 BREEDING)	70
12 AI FIRST SERVICE PREGNANCY RATE WHEN BRED TO AN OBSERVED ESTRUS IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975 BREEDING)	71
13 AI FIRST SERVICE CONCEPTION RATE WHEN BRED NONESTRUS AND RECEIVED PGF2 α (ALL 1975 BREEDING)	72
14 THE EFFECT OF THE SECOND INJECTION OF PGF2 α AT THE 80 HR NONESTRUS BREEDING ON ESTRUS AND PREGNANCY RATES (ALL 1975 BREEDING)	73
15 PERCENT OF BEEF CATTLE PREGNANT THE FIRST TEN DAYS OF THE AI BREEDING SEASON WITH ONE AI SERVICE IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975 BREEDING)	74
16 THE AVERAGE DAY OF CONCEPTION IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (AI AND SUBSEQUENT NATURAL BREEDING SEASON INCLUDED) (ALL 1975 BREEDING)	75
17 TOTAL PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 AND 1975 BREEDING)	86
18 TOTAL AI PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 AND 1975 BREEDING)	87
19 AI FIRST SERVICE PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 AND 1975 BREEDING)	88
20 AI FIRST SERVICE PREGNANCY RATE WHEN BRED TO AN OBSERVED ESTRUS IN A PGF2 α BREEDING SYSTEM (ALL 1974 AND 1975 BREEDING)	89

Table	Page
21 AI FIRST SERVICE CONCEPTION RATE WHEN BRED NONESTRUS AND RECEIVED PGF2 α (ALL 1974 AND 1975 BREEDING)	90
22 PERCENT OF BEEF CATTLE PREGNANT THE FIRST TEN DAYS OF THE AI BREEDING SEASON WITH ONE AI SERVICE IN A PGF2 BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 AND 1975 BREEDING)	91
23 THE AVERAGE DAY OF CONCEPTION IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (AI AND SUBSEQUENT NATURAL BREEDING SEASON INCLUDED) (ALL 1974 AND 1975 BREEDING)	91
24 THE EFFECT OF THE SECOND INJECTION OF PGF2 α AT THE 80 HR NONESTRUS BREEDING ON TOTAL PREGNANCY RATE (ALL 1975 BREEDING).	92
25 THE EFFECT OF THE SECOND INJECTION OF PGF2 α AT THE 80 HR NONESTRUS BREEDING ON TOTAL AI PREGNANCY RATE (ALL 1975 BREEDING)	94
26 THE EFFECT OF THE SECOND INJECTION OF PGF2 α AT THE 80 HR NONESTRUS BREEDING ON AI FIRST SERVICE PREGNANCY RATE (ALL 1975 BREEDING)	95

INDEX TO FIGURES

Figure	Page
1 PRINCIPLE ENDOCRINE PATHWAYS INVOLVED IN THE CONTROL OF OVARIAN FUNCTION.	5
2 POSSIBLE MECHANISMS OF PROSTAGLANDIN $F_2\alpha$ INDUCED LUTEOLYSIS	33
3 FORMAT FOR THE PGF2 α AND CONVENTIONAL AI BREEDING SYSTEMS	50
4 PERCENT OF THE HERD PREGNANT PER DAY OF THE AI SEASON FOR THE PGF2 α AND CONVENTIONAL BREEDING SYSTEMS FOR THE 1974 COMBINED ANALYSIS	96
5 PERCENT OF THE HERD PREGNANT PER DAY OF THE AI SEASON IN THE PGF2 α AND CONVENTIONAL BREEDING SYSTEMS FOR THE 1975 COMBINED ANALYSIS	97
6 AI FIRST SERVICE PREGNANCY RATE (CATTLE INSEMINATED TO ESTRUS AND NONESTRUS) vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE 1974 AND 1975 BREEDING SEASON (COMBINED ANALYSIS).	98
7 ESTRUS RESPONSE OF PGF2 α TREATED CATTLE vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE 1974 AND 1975 BREEDING SEASON (COMBINED ANALYSIS).	99
8 AI FIRST SERVICE PREGNANCY RATE OF CATTLE INSEMINATED TO AN OBSERVED ESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE 1974 AND 1975 BREEDING SEASON (COMBINED ANALYSIS).	100
9 AI FIRST SERVICE PREGNANCY RATE OF CATTLE INSEMINATED NONESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE 1974 AND 1975 BREEDING SEASON (COMBINED ANALYSIS)	101

INDEX TO APPENDIX FIGURES

Figure	Page
1 ESTRUS RESPONSE OF PGF2 α TREATED CATTLE vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE SPRING 1975 BREEDING SEASON	103
2 AI 1st SERVICE PREGNANCY RATE OF CATTLE INSEMINATED TO AN OBSERVED ESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE SPRING 1975 BREEDING SEASON	104
3 AI 1st SERVICE PREGNANCY RATE OF CATTLE INSEMINATED NONESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE SPRING 1975 BREEDING SEASON.	105
4 ESTRUS RESPONSE OF PGF2 α TREATED CATTLE vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR 1st CALF HEIFERS IN THE FALL 1975 BREEDING SEASON.	106
5 AI 1st SERVICE PREGNANCY RATE OF CATTLE INSEMINATED TO AN OBSERVED ESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR 1st CALF HEIFERS IN THE FALL 1975 BREEDING SEASON.	107
6 AI 1st SERVICE PREGNANCY RATE OF CATTLE INSEMINATED NONESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR 1st CALF HEIFERS IN THE BREEDING SEASON.	108
7 ESTRUS RESPONSE OF PGF2 α TREATED CATTLE vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE FALL 1975 BREEDING SEASON	109
8 AI 1st SERVICE PREGNANCY RATE OF CATTLE INSEMINATED TO AN OBSERVED ESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE FALL 1975 BREEDING SEASON.	110
9 AI 1st SERVICE PREGNANCY RATE OF CATTLE INSEMINATED NONESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE FALL 1975 BREEDING SEASON	111

Figure	Page
10 ESTRUS RESPONSE OF PGF2 α TREATED CATTLE vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE FALL 1974 BREEDING SEASON.	112
11 AI 1st SERVICE PREGNANCY RATE OF CATTLE INSEMINATED TO AN OBSERVED ESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE FALL 1974 BREEDING SEASON.	113
12 AI 1st SERVICE PREGNANCY RATE OF CATTLE INSEMINATED NONESTRUS vs. DAYS POSTPARTUM ON THE DAY OF PGF2 α INJECTION FOR MATURE COWS IN THE FALL 1974 BREEDING SEASON.	114

ABSTRACT

Breeding studies were conducted utilizing $\text{PGF}_{2\alpha}$ 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. heifers, $n=87$), (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 $\text{PGF}_{2\alpha}$ 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 $\text{PGF}_{2\alpha}$ system were observed for estrus and bred from day $-\frac{1}{2}$ to 4 at which time the remaining cattle were injected IM with 33.5 mg $\text{PGF}_{2\alpha}$ THAM-salt. At 72 hr (groups 1, 2 and 3) or 80 hr (groups 4, 5, 6 and 7) post-injection, all $\text{PGF}_{2\alpha}$ 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 category were reinjected with 33.5 mg of $\text{PGF}_{2\alpha}$ immediately after insemination. Conception dates were confirmed based on actual calving dates. The total pregnancy rate (combined analysis, groups 1 through 7) for the $\text{PGF}_{2\alpha}$ system was significantly higher (78 vs 72%, $P=0.185$) than in the conventional system. The total AI pregnancy rate (combined analysis) for the $\text{PGF}_{2\alpha}$ 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 $\text{PGF}_{2\alpha}$ system than in the conventional breeding system. This resulted in the average day of conception being 5 days earlier in the $\text{PGF}_{2\alpha}$ 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 $\text{PGF}_{2\alpha}$ treated cattle that were between 69 and 80 days postpartum on the day $\text{PGF}_{2\alpha}$ was administered. The cattle receiving the second injection of $\text{PGF}_{2\alpha}$ 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 luteolytic 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.

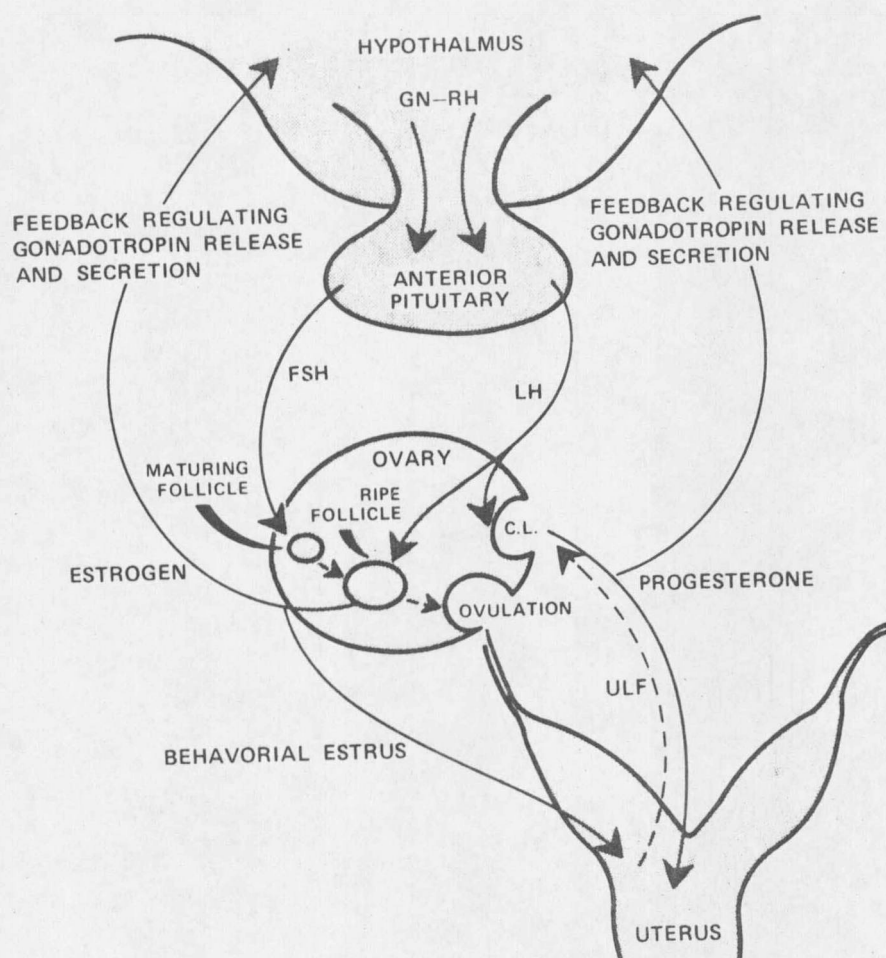


Figure 1. Principle endocrine pathways involved in the control of ovarian function.

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 corpora 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 lutolytic 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 intraperitoneally 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 hypophyseal 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 alone 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 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 significantly 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. $\text{PGF}_{2\alpha}$ 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 $\text{PGF}_{2\alpha}$ the ULF?

As stated by Pharris et al. (1972), for prostaglandin $\text{F}_{2\alpha}$ to be the endogenous luteolytic factor, five criteria would have to be satisfied (1) $\text{PGF}_{2\alpha}$ 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) $\text{PGF}_{2\alpha}$ 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 $\text{PGF}_{2\alpha}$ and (5) the luteolysis induced by $\text{PGF}_{2\alpha}$ should mimic spontaneous luteolysis, biochemically, morphologically and

functionally.

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

Pharris and Wyngarden (1969) infused prostaglandin F_{2α} 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_{2α} on pseudopregnant rabbits. Prostaglandin F_{2α} (5 mg/kg/day) was given on days 4 through 8 of pseudopregnancy, and the ovaries were collected on day 12. PGF_{2α} 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_{2α} 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_{2α} 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_{2α}

would cause luteal regression. The dose levels ranged from 0.01 to 100.0 ug/hr and were administered via the cannulated left carotid artery.

LaVoie et al. (1975) totally hysterectomized 8 cows between 9 and 13 days after estrus. Cows were divided into either the $\text{PGF}_{2\alpha}$ treatment or the control. $\text{PGF}_{2\alpha}$ treated cows had reduced serum progesterone concentration and significantly smaller weights and diameters when compared to control. The weights and diameters of corpora lutea were significantly smaller than those from controls. These results demonstrated that $\text{PGF}_{2\alpha}$ is luteolytic in hysterectomized cows.

Lauderdale (1972) demonstrated $\text{PGF}_{2\alpha}$ to be luteolytic in intact cows. $\text{PGF}_{2\alpha}$ -THAM salt (30 mg) was injected subcutaneously on one of the following days after estrus. Group A (days 2, 3, 4) demonstrated essentially normal cycle lengths. Group B (days 6, 7, 8, 9) and Group C (days 13, 14, 15, 16) responded with estrus 2 to 4 days following injection.

Rowson et al. (1972) found normal corpus luteum regression after injecting 0.5 mg/day of $\text{PGF}_{2\alpha}$ to cattle between days 5 and 16 of their estrous cycle. The same dosage given from days 1 to 4 was not effective in causing CL regression or decreasing the cycle length. These findings indicate that $\text{PGF}_{2\alpha}$ is luteolytic in cattle only between days 5 to 16 of the cycle which coincides with the time when the CL is fully functional. Cattle in days 17 to 21 of their cycle were coming into estrus thus the endogenous luteolysin had previously been released.

Liehr et al. (1972) studied the effects of $\text{PGF}_{2\alpha}$ on blood progesterone levels and estrous cycle length of beef heifers (500 ug intra-uterine infusion). The average cycle length was 11.4 days in the ipsilaterally treated as opposed to 15.2 days in the contralaterally treated heifers. Progesterone levels dropped to nondetectable levels within 2 days after ipsilateral $\text{PGF}_{2\alpha}$ treatment, however remained relatively high in contralateral $\text{PGF}_{2\alpha}$ treatment. These results indicate that $\text{PGF}_{2\alpha}$ is luteolytic in beef heifers, when given in low doses, and is effective on a local basis.

Inskeep (1973) reported that exogenous $\text{PGF}_{2\alpha}$ caused luteal regression in sheep with functional corpora lutea in ovaries transplanted to the neck or in cattle during day 5 through 18 of the estrous cycle and during pregnancy.

Lamond et al. (1973) studied the effects of administering $\text{PGF}_{2\alpha}$ into the lumen of the uterus, into the uterine artery, or into the jugular vein in pregnant and luteal phase cows. Luteolysis occurred, followed by abortion or reduction in the length of the estrous cycle.

Louis et al. (1973) injected 30 mg $\text{PGF}_{2\alpha}$ -THAM salt IM into 5 heifers that were between days 9 to 13 of the estrous cycle and into 6 heifers in day 3 of the estrous cycle and intravaginally into 6 heifers during diestrus. Corpus luteum diameter decreased, blood serum progesterone fell and estrus began at about 74 hr[±]3 hr after administration in all animals.

Stellflug et al. (1973) administered $\text{PGF}_{2\alpha}$ in 30 mg doses, two 15 mg doses at 6 hr intervals or 60 mg doses, to 11 heifers in each case. Progesterone levels dropped and did not differ significantly among the three treatments. The interval to estrus did not significantly differ between treatments.

These studies demonstrate $\text{PGF}_{2\alpha}$ to be luteolytic in rats, rabbits, guinea pigs, sheep and cattle in all of which the uterus is implicated in luteal function.

2. "Prostaglandins must cause luteolysis when administered systemically and on a local basis".

Prostaglandin $\text{F}_{2\alpha}$ has been demonstrated to be luteolytic when administered systemically to the rat (Pharris and Wyngarden, 1969), rabbit (Pharris, 1970), guinea pig (Blatchley and Donovan, 1969) hamster (Gutknecht et al., 1971), ewe (McCracken et al., 1970), cow (LaVoie et al., 1975; Stellflug et al., 1973; Lauderdale, 1972) and the mare (Douglas and Ginther, 1972).

Goding et al. (1972) presented initial evidence that $\text{PGF}_{2\alpha}$ is luteolytic on a local basis in the ewe when given at sub-threshold doses (doses not luteolytic when given other than locally). They infused $\text{PGF}_{2\alpha}$ into the uterine vein on the same side as the ovary bearing the CL in 6 sheep between days 7 to 8 of their estrous cycle. In their analysis approximately 20 ug/hr was suggested to be the minimum effective dose. It was found that luteolysis occurred in

all ewes at all doses with the exception of one ewe which received the 20 ug/hr dose for 7 hr.

Liehr et al. (1972) and Lamond et al. (1973) demonstrate exogenous $\text{PGF}_{2\alpha}$ to be luteolytic in the cow when administered on a local basis. This data supports the hypothesis that the luteolysin ($\text{PGF}_{2\alpha}$) is delivered via a local mechanism rather than being released into the general circulation. In support of the idea of a local mechanism is the fact that $\text{PGF}_{2\alpha}$ is rapidly cleared from the general circulation by the lungs and the liver.

McCracken et al. (1972) tested a counter-current hypothesis between the uterine vein and ovarian artery using ^3H -labelled $\text{PGF}_{2\alpha}$ in an attempt to explain the localized effect. The labelled $\text{PGF}_{2\alpha}$ was infused at a constant rate into the uterine vein before the point at which it joins the utero-ovarian vein. Samples of ovarian arterial blood were collected at the hilus of the ovary and compared to samples collected simultaneously from the iliac artery. $\text{PGF}_{2\alpha}$ in the ovarian arterial blood increased markedly, while $\text{PGF}_{2\alpha}$ in the iliac arterial samples showed only a small increase, indicating direct transfer of the labelled prostaglandin from the uterine vein to the ovarian artery. This concept provides a possible explanation for the local utero-ovarian effects that have been observed.

Previous discussion on the local effects of $\text{PGF}_{2\alpha}$ in studies with rabbits, ewes and cows, evidenced is presented demonstrating

PGF_{2α} to be luteolytic when administered via a local route.

3. "PGF_{2α} must be present in or released from the endometrium at a time consistent with uterine induced luteolysis".

Poyser et al. (1971) sacrificed 35 guinea pigs on day 3 of the estrous cycle. One uterine horn from each was used for distention and the other served as a control. Biochemical analysis revealed that PGF_{2α} was present in all cases. These results, coupled with the known luteolytic properties of PGF_{2α}, are strong evidence for PGF_{2α} as the uterine luteolysin in guinea pigs.

In previous discussion it was indicated that estradiol treatments caused luteolysis. This is presumably by initiating the release of the luteolytic factor from the uterus. Blatchley et al. (1971) performed an experiment which tested the hypothesis that PGF_{2α} is the luteolysin. Guinea-pigs were injected subcutaneously with 10 ug of estradiol benzoate per day from days 4 to 6 of the cycle (day 1=estrus). Plasma taken from the control or estrogen-treated hysterectomized animals contained no detectable prostaglandin F_{2α}. This would be expected as luteolysis after estradiol treatment has been demonstrated not to occur in hysterectomized animals (Brunner et al., 1969). In the treatment containing the intact guinea pigs the results revealed an increase in PGF_{2α} (300%) in the estrogen injected animals.

To coincide with the natural cycle $\text{PGF}_{2\alpha}$ would have to be either undetectable or at base line levels during the cycle until the time just before natural corpus luteum regression begins. At this time, a rise in $\text{PGF}_{2\alpha}$ levels should be seen. Wilson et al. (1972) looked at levels of $\text{PGF}_{2\alpha}$ in ewes at various days of the cycle. The endometrium from each uterine horn of 35 mature ewes with known corpora lutea on only one ovary were studied. The ewes were in four groups and were killed on day 3, 5, 11 or 14 of the estrous cycle. The mean concentration of $\text{PGF}_{2\alpha}$ in ng/g for both uterine horns was 32, 60, 76 and 202 and the mean $\text{PGF}_{2\alpha}$ content (ng) was 261, 344, 311 and 1244, respectively, with levels at day 14 being significantly greater ($P < .05$) than all other days.

Evidence presented indicating that $\text{PGF}_{2\alpha}$ is present in the uterus at times consistent with uterine induced luteolysis is substantial and supports the role of $\text{PGF}_{2\alpha}$ in cases where luteolysis is induced via the uterus and during normal cycling.

4. "Pregnancy should counteract the presence or action of $\text{PGF}_{2\alpha}$ ".

Rowson and Moor (1967) found that daily intrauterine infusions of a tissue homogenate prepared from 14 or 15 day sheep embryos resulted in an extension of the estrous cycle. It was suggested that a substance from the embryonic tissue probably acts on the endometrium in an anti-luteolytic manner. The exact mechanism by which the embryo

over comes the luteolytic effect of the uterus is not known. However, pregnancy does result in prolongation of the functionality of the corpus luteum in the cow and ewe.

The area of how pregnancy counteracts $\text{PGF}_{2\alpha}$ is indeed in question as yet.

5. "The luteolysis induced by $\text{PGF}_{2\alpha}$ should mimic spontaneous luteolysis, biochemically, morphologically and functionally".

Pharris and Wyngarden (1969) observed in rats following $\text{PGF}_{2\alpha}$ a shift from progesterone to 20-dihydroprogesterone dominance. In addition estrus occurred and a disorganization of luteal cells typical of luteal degeneration was evident. LaVoie et al. (1975) observed a decrease in progesterone levels, corpus luteum regression, the occurrence of estrus and the evidence of ovulation and new corporal lutea formation in $\text{PGF}_{2\alpha}$ treated hysterectomized cows. The same sequence of events are seen (estrus, ovulation and corpus luteum formation) in the natural occurring cycles of intact cows (LaVoie et al., 1975).

The previously described regressive changes in the bovine corpus luteum are closely related to changes (decreases) in the progesterone content (Donaldson and Hansel, 1965) all of which were demonstrated to occur in the cow following administration of $\text{PGF}_{2\alpha}$.

Prostaglandins

A brief history. Goldblatt (1933) described the smooth muscle stimulating activity caused by extracts of human seminal fluid. These findings were also observed by Von Euler (1934), and in 1936 he gave the name prostaglandin to this new substance in belief that it originated in the prostate gland. In 1959, Eliasson proved that human seminal prostaglandins originate from the seminal vesicles rather than the prostate glands. The pharmacological activity of human seminal fluid was recognized many years before the discoveries by Goldblatt or Von Euler.

Chau (1972) indicates that in ancient China, human seminal fluid was considered to be the therapeutic value in patients with gastric ulcers (as reviewed by Karim, 1975).

Harley (1941) describes oral ingest of human semen to induce labor in North African Tribes (as reviewed by Karim, 1975).

Japelli and Scafa (1906) observed a rise in blood pressure in the dog following injection of extracts from bull and dog prostate glands (as reviewed by Karim, 1975).

Lauderdale (1974) demonstrated that prostaglandins are found or have been detected in most mammalian body tissues.

Basic chemistry and biosynthesis of prostaglandins. As reviewed by Karim (1975), prostaglandins are 20-carbon hydroxy fatty acids with a cyclopentane ring and two side-chains and are derivatives of

prostanoic acid. There are four groups of prostaglandins designated by the letters, E, F, A and B. This designation is related to differences in the five-membered cyclopentane ring. The primary prostaglandins are the E's and F's, while the A's and B's are derivatives from the primaries. The degree of unsaturation is denoted by the subscript number after the letter. The α -isomers are the only naturally occurring prostaglandins. The biosynthetic precursors for prostaglandins are linoleic acid, arachidonic acid and pentanoic acid. A microsomal synthetase system (prostaglandin synthetase) controls the natural synthesis of prostaglandins from their fatty acid precursors. Non-steroidal anti-inflammatory drugs such as aspirin, indomethacin and fenamates inhibit prostaglandin synthetase activity, which is found in many organs.

Caribbean coral contains 15-epi-PGA_{2 α} and its diester in amounts of 0.1 and 1.3%, respectively, in the dried cortex. Coral prostaglandins have been used as intermediates to prepare biologically active natural prostaglandins (Weinshenker and Andersen, 1973; Schneider, 1975).

Karim (1975) indicates that over 90% of PGE and PGF compounds are metabolized during one circulation through the lungs and liver. This is evidence for these compounds to be more important as local hormones while the A and B series are metabolized less rapidly and may be more important as circulating hormones.

Prostaglandins have been shown to have many physiological effects and when dealing specifically with reproduction in the male, they are

implicated in the process of erection, ejaculation, sperm motility and morphology. In the female the accumulated evidence suggests that prostaglandins are involved in menstruation, spontaneous abortion, labour, ovulation and luteolysis (Karim, 1975).

The mechanism of action of $\text{PGF}_{2\alpha}$. The precise mechanism of $\text{PGF}_{2\alpha}$ induced luteolysis is not known, however, Pharris et al. (1972) discusses five possibilities. Figure 2 from Pharris et al. (1972) depicts the five possible mechanisms of $\text{PGF}_{2\alpha}$ induced luteolysis.

Postulate One ($\text{PGF}_{2\alpha}$ blocks the pituitary or luteotropic complex).

With the pituitary gland being important in maintenance of luteal activity, it was first suspected as the site of $\text{PGF}_{2\alpha}$ activity. The position taken was the $\text{PGF}_{2\alpha}$ blocked the pituitary totally or at least the luteotropic complex from the pituitary (figure 1, #1). $\text{PGF}_{2\alpha}$ is luteolytic only on fully functioning corpora lutea (Rowson et al., 1972). Lauderdale (1972) found that $\text{PGF}_{2\alpha}$ is not luteolytic in the bovine CL during the first 4 days of the estrous cycle and is luteolytic from days 5 to 16 of the cycle.

Pharris et al. (1972) indicates that LH levels are unaffected by $\text{PGF}_{2\alpha}$ treatment as revealed by hormone assay. Low doses of $\text{PGF}_{2\alpha}$ when given systemically in the cow are ineffective in causing luteolysis, however, the same dose given in the ovarian artery is effective in causing luteolysis. These kinds of results indicate strongly that the pituitary or the hypothalamus are not involved in the luteolytic

mechanism of $\text{PGF}_{2\alpha}$. This reasoning is reinforced when one considers previous discussion stating that most $\text{PGF}_{2\alpha}$ is cleared from the circulation in one pass through the lungs and liver.

Postulate Two ($\text{PGF}_{2\alpha}$ stimulates the uterus to release luteolysin).

$\text{PGF}_{2\alpha}$ is a strong smooth muscle stimulator. It was thought that $\text{PGF}_{2\alpha}$ might stimulate the uterus to release (via smooth muscle stimulation) some endogenous luteolysin (figure 2, #3).

LaVoie et al. (1975) demonstrated that $\text{PGF}_{2\alpha}$ was luteolytic in hysterectomized cows which implies that the uterus is not necessary for $\text{PGF}_{2\alpha}$ to induce CL regression.

This postulate is disproven in the cow by virtue of the fact that $\text{PGF}_{2\alpha}$ is luteolytic in hysterectomized cows.

Postulate Three ($\text{PGF}_{2\alpha}$ has a direct toxic effect of the CL). A direct toxic effect by $\text{PGF}_{2\alpha}$ on the corpus luteum is another possible mode of action for $\text{PGF}_{2\alpha}$ (figure 2, #4). Henderson and McNatty (1975) and O'Grady (1972) indicates that PGF_2 inhibits secretion of progesterone by luteal tissue in vitro. The implication here is that $\text{PGF}_{2\alpha}$ is exerting a direct biochemical effect on the luteal cells which is causing cessation of progesterone synthesis. Rowson et al. (1972) and Lauderdale et al. (1972) have shown that $\text{PGF}_{2\alpha}$ is not effective on CL of the cow up to day 5 of the estrous cycle. The possibility exists that the pre-ovulatory LH surge saturates the regulatory units of the luteal cells thus protecting the newly developed CL from PGF_2

(Henderson and McNatty, 1975).

The available literature is not conclusive in answering the question of whether the mechanism of $\text{PGF}_{2\alpha}$ induced luteolysis is via a direct toxic effect on the CL.

Postulate Four ($\text{PGF}_{2\alpha}$ exerts an antigonadotropic action). A fourth possible method is that $\text{PGF}_{2\alpha}$ performs an antigonadotropic action (figure 2, #2). It is possible that $\text{PGF}_{2\alpha}$ could interact with LH or FSH in the circulation or at the receptor site on the corpus luteum. Pharris et al. (1972) presented data which showed that the ovarian effects of HCG and PMS which have LH and FSH like activity, respectively, can be overcome by simultaneous injection of $\text{PGF}_{2\alpha}$. Hichens et al. (1974) indicated the $\text{PGF}_{2\alpha}$ may cause a reduced hormone binding capacity at binding sites on the CL.

The previous discussion suggest that $\text{PGF}_{2\alpha}$ is antagonistic to luteotropins and remains as a possible mechanism of $\text{PGF}_{2\alpha}$ induced luteolysis.

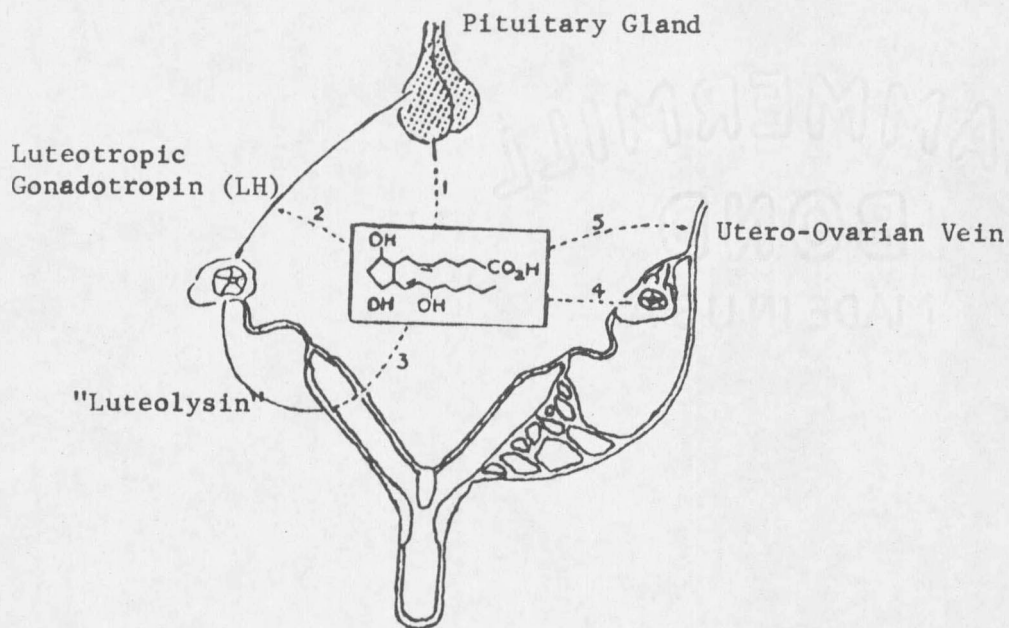
Postulate Five ($\text{PGF}_{2\alpha}$ caused constriction of the utero-ovarian vein). The fifth possible mechanism is constriction of the utero-ovarian vein (figure 2, #6). Pharris (1970) indicates that in rats after a single dose of $\text{PGF}_{2\alpha}$, there is an immediate drop in blood flow of 50 to 60% of control levels, lasting about 25 minutes. Ginther and Bisgard (1972) presented evidence of uterine luteolytic activity by the uterine vein in the ewe. An intrauterine device (IUD) was placed in the horn

of the uterus contralateral to the active corpus luteum and the ipsilateral uterine horn was removed. The corpora lutea of these animals were maintained because of the absence of the ipsilateral uterine horn. In ewes where the uterine vein from the IUD bearing horn, was successfully anastomosed to the utero-ovarian vein of the opposite ovary bearing the CL, regression occurred.

The mechanism of $\text{PGF}_{2\alpha}$ induced luteolysis is still not fully resolved. There are however, several supportable hypothesis (1) a direct toxic effect on the CL (2) gonadatrophin antagonism (3) alteration of ovarian blood flow.

Estrus Synchronization

Methods of estrus synchronization in farm animals and specifically cattle have been attempted for a long time. In a random herd of cows, 5% per day will be in estrus if 100% are cycling. A conventional artificial insemination (AI) program requires larger amounts of labor for estrus detection. Successful estrus synchronization would reduce the necessity for estrus detection. In early estrus synchronization attempts, exogenous progesterone was given for various lengths of time and then withdrawn allowing the surge of LH to occur in all animals at approximately the same time.



- 1 = direct feedback on pituitary gland
 - 2 = antigonadotropic effect
 - 3 = stimulation of uterus to produce luteolysin
 - 4 = direct toxicity of corpus luteum
 - 5 = constriction of utero-ovarian vein.
- From Behrman et al., Ann. N.Y. Acad. Sci. 180, 437 (197). In. Pharris et al., (1972).

Figure 2. Possible mechanisms of prostaglandin $F_2\alpha$ in luteolysis.

Exogenous steroid therapy. Christian and Casida (1948) injected 50 mg of progesterone (in corn oil) per day into heifers. Injections started on day 14 of the estrous cycle and continued for 14 days. All heifers exhibited estrus 5 to 6 days after the last progesterone injection. It was concluded that exogenous progesterone treatments synchronized the heifers by suppressing estrus and ovulation and allowing all animals to progress to approximately the same stage of the cycle.

Willett (1950) found that 11 pregnancies resulted from 22 breedings after synchronization of estrus using progesterone. Injections of 50 to 100 mg of progesterone were administered to heifers for 13 to 17 days. After termination of injections, the heifers were observed for estrus and artificially inseminated at the first post treatment estrus and again 24 hr later. Fifty percent conception was reported for treated animals and no results were given for controls.

Trimberger and Hansel (1955) found that when using dosages of 50, 75 or 100 mg of progesterone (subcutaneously) for 14 days that only 12.5% of the treated cows conceived as compared to 64% of the controls (no length of breeding season reported for controls) when using natural service.

Ulberg and Lindley (1960) studied the effects of progesterone levels varying from 12.5 mg to 50 mg in cows. Progesterone was administered for 14 consecutive days. Estradiol benzoate (0.5 to 1.0 mg) was given 3 days after the last progesterone injection. Eighty-six percent

percent (291/333) of the cows were exhibiting estrous 2.5 to 9.5 days after treatment. First service conception rates were 26% and 51% for the treated and controls, respectively. It was reported that estrogen eliminated much of the variation in time in the onset of estrus, after progesterone administration.

Wiltbank et al. (1965) studied the effect of injections (IM) of progesterone alone or in combination with estrogen compounds on the bovine estrus cycle. Cycling heifers were treated with 24 daily injections of 20 mg of progesterone (n=19) alone or in combination with 10 (n=20), 20 (n=19) or 40 (n=20) ug of estradiol or 40 mg of progesterone alone (n=20) or with 20 (n=20), 40 (n=19) or 80 (n=19) ug of estradiol. The two remaining treated groups received the same progesterone treatment (either 20 mg, n=20 or 40 mg, n=19) plus three injections of estradiol (20 mcg) on the 23rd, 24th and 25th days. Group 1, an additional group (n=20), served as the control. From 70 to 100% of all treated heifers exhibited estrus in a 4-day period after treatment was discontinued. It was found that IA first service fertility was significantly lower in heifers receiving treatments (28%) as compared to controls (60%).

Daily injections of livestock is not a practical management procedure. With this in mind, the idea of oral application of progesterone or progesterone plus estrogen arose. This was followed by the use of implants and/or impregnated pessaries (Nellor et al., 1960; Nelms and

Combs, 1961; Hansel and Malven, 1960; Hansel et al., 1961; Fahning et al., 1966; Dhindsa et al., 1967). In general, lowered first service conception rates were observed when compared to control rates although synchronization rates were generally good.

Burrell et al. (1972) used ear implants of 19 alpha acetoxy 11 beta-methyl 19 norpreg 4 ene3, 2 dione (SC21009) in heifers. The implants (5 mg SC21009) plus 5 mg of estradiol valerate (trials 1 and 2) and 7.5 mg estradiol valerate (trial 3) IM were administered simultaneously. SC21009 implants remained intact for 9 days. Heifers exhibited estrus within 4 days of implant removal (88, 90 and 94% for trials 1, 2 and 3, respectively). First service pregnancy rates for the 9 day treated heifers were 62, 50 and 40% (trials 1, 2 and 3, respectively) as compared to 71, 61 and 64% for controls (trials 1, 2 and 3, respectively, not significantly different).

Wishart and Young (1974) used SC21009 and Whitman et al. (1972) used SC21009 plus varying levels of estradiol valerate to synchronize estrus in cows. Fertility was reported to be comparable to controls.

Another approach to manipulating the estrus cycle in cows is by manual enucleation of the corpus luteum as indicated by Inskeep (1973). This method is dangerous because it can cause excessive hemorrhage as well as being impractical to use on a herd basis due to the time involved and technical skill required.

An alternate approach would be to chemically regress the corpus luteum.

Synchronization with $\text{PGF}_{2\alpha}$. As previously discussed, prostaglandin $\text{F}_{2\alpha}$ has been shown to be luteolytic in the ewe (McCracken et al., 1972), cow (Lauderdale, 1972), mare (Douglas and Ginther, 1972) and sow (Diehl and Day, 1973).

Stellflug et al. (1973) and Stellflug et al. (1975) have demonstrated that single dosages of 60 mg, 30 mg or double dosages of 15 mg at 6 hr intervals were all luteolytic, however the difference in dose level did not significantly effect the decline in blood progesterone the increase in blood estradiol, the duration or the peak of the LH surge, the interval to onset of estrus, nor the interval to ovulation in cattle.

Rowson et al. (1972) found that when $\text{PGF}_{2\alpha}$ was injected non-surgically into the ipsilateral uterine horn of cattle, CL regression occurred at a dose level of 0.5 mg/day on two consecutive days.

Welch et al. (1975) studied the effects of $\text{PGF}_{2\alpha}$ and of estradiol benzoate on estrus and conception in 67 lactating beef cows. $\text{PGF}_{2\alpha}$ was infused into the uterus in two trials (1 mg in trial 1 and 2 mg in trial 2). Forty-three hr after $\text{PGF}_{2\alpha}$ treatment approximately half of these cattle received 400 ug of estradiol benzoate. The data for trials was pooled as differences between trials was not significant. Over both trials pregnancy rates were 61, 73, 56 and 71% for the $\text{PGF}_{2\alpha}$,

PGF_{2α} plus estradiol benzoate, sham-infused control and the untreated controls, respectively. They concluded that intrauterine administration of PGF_{2α} was effective in controlling estrus.

Hafs et al. (1974) deposited 5 mg PGF_{2α} into the uterus of cows during diestrus and observed that progesterone fell 50% within 12 hr, estradiol more than doubled within 24 hr, LH peaked at 71 hr, estrus began at 72 hr and ovulation occurred at 95 hr post-treatment. Fertility of cattle inseminated 12 hr after the onset of estrus following treatment with PGF_{2α} and that of cattle inseminated twice at 72 and 90 hr after PGF_{2α} was equivalent to that in controls.

Hearnshaw et al. (1974) and Henricks et al. (1974) demonstrated that only 5 mg of PGF_{2α} was required to cause CL regression when administered by intrauterine infusion to cows.

Lauderdale (1972) found that a subcutaneous dose of 30 mg of PGF_{2α}-THAM salt would cause regression of the corpus luteum in cattle between days 6 and 16 of their cycle.

Lauderdale et al. (1974) demonstrated that PGF_{2α} was effective when used for estrus synchronization on a large scale. Cattle were assigned to one of three treatments at four locations. Treatment group 1 (n=153) was the control in which the animals were observed for estrus and inseminated during an 18 to 25 day interval. Animals in groups 2 (n=119) and 3 (n=120) were injected with 30 mg of PGF_{2α}-THAM salt if a CL was detected by rectal palpation or assumed to be present based on

a previous palpation. Cattle in group 2 were observed for estrus and inseminated during days 1 through 7 after $\text{PGF}_{2\alpha}$ treatment. Cattle in group 3 were inseminated twice, once at 72 hr and again at 90 hr after PGF_2 without regard to estrus. For treatments 1, 2 and 3, the percent pregnant was 53.3, 52.2 and 55.8%, respectively, (differences not significant).

Roche (1974) assigned 33 heifers that were between days 5 and 20 of their estrous cycles to either group 1, (control, n=11) group 2, (30 mg $\text{PGF}_{2\alpha}$ IM n=11) and group 3, (20 mg $\text{PGF}_{2\alpha}$ IM n=11). All heifers were inseminated to an observed estrus until all control heifers had been inseminated once. The percent pregnant 73, 75 and 70% for groups 1, 2 and 3, respectively. There was no significant differences in fertility among groups, and in the treated groups neither the dosage nor stage of the cycle when given, influenced the estrus response.

Roche (1974) also discussed that an estrus synchronization system that accounts for only those cattle in days 5 to 17 of their cycle is impractical for use in a production situation. It was suggested that two doses of $\text{PGF}_{2\alpha}$ administered 10 days apart should synchronize all cycling cattle within a random herd. Cattle in days 5 to 17 should be in estrus shortly after the first injection and at about day 7 of their next cycle at the time of the second $\text{PGF}_{2\alpha}$ treatment. Cattle that are in days 17 to 21 of their cycle should have normal estrus at the time of the first treatment and be at about days 7 to 10 of

their next cycle at the time of the second injection. Cattle in days 1 to 5 at the time of the first injection should have been in estrus prior to treatment one and should be at approximately day 10 to 14 at the second injection.

A two injection system such as the one previously described was first tried by King and Robertson (1974). Two injections of $\text{PGF}_{2\alpha}$ were given 10 days apart to 30 randomly cycling Holstein heifers. Twenty-five of 30 heifers (83%) exhibited estrus and were inseminated 2 to 4 days after the second injection and 10 of the 25 (40%) were pregnant 60 days after insemination. In the control 13 of 15 (87%) were detected in estrus during a 3-week period and 7 of 13 or 54% were found pregnant at 60 days. It was concluded that the double injection system may have commercial application as the number pregnant was not significantly different from controls.

Hafs et al. (1975) tested fertility of 960 heifers and 392 suckled cows after AI in 36 commercial herds. Assignments of cattle were as non-treated controls (group 1) or injected twice (10 to 12 days apart) with 30 mg $\text{PGF}_{2\alpha}$ -THAM salt (group 2) or receiving .5 mg ICI 80, 996 (group 3). $\text{PGF}_{2\alpha}$ treated cattle were inseminated either once at 80 hr or twice at 70 and 88 hr after the second injection without estrus detection. The results were 51% of the 346 control heifers (group 1 heifers) exhibited estrus with 67% conceiving (1st service). Sixty-two percent of the 291 heifers inseminated twice conceived and 62% of the

323 heifers inseminated once conceived. One hundred-thirteen of 133 control cows showed estrus of which 69% conceived (1st service). Of 102 treated cows inseminated twice 58% conceived and 57% of the 157 cows inseminated once conceived. No length for the breeding season was reported. It was found that fertility was not different between treated and control animals. There were no significant differences between animals inseminated once and those inseminated twice.

An alternative to the double injection system of $\text{PGF}_{2\alpha}$ administration would be utilization of a single injection system by manipulating cattle in days 0 to 5 of their estrous cycle. This could be accomplished by suppressing estrus in all cattle and at the same time allowing all cattle to progress to a physiological state where $\text{PGF}_{2\alpha}$ will cause luteolysis. At this point, the estrus suppressing agent could be removed and $\text{PGF}_{2\alpha}$ administered.

Heersche et al. (1974) combined the progesterone implant SC21009 with $\text{PGF}_{2\alpha}$. In this experiment, 6 mg SC21009 implants were placed in 50 heifers and removed after 7 days. Thirty mg of $\text{PGF}_{2\alpha}$ was injected at that time to each heifer. Estrus was observed and insemination occurred about 12 to 18 hr later. By 84 hr post-injection 47 of 50 were in estrus with 63.8% conceiving to first service compared to 65% in an untreated control group over a period of 27 days.

A 6 mg SC21009 implant was used by Wishart (1974) for 5 days followed by 3.0 mg of $\text{PGF}_{2\alpha}$ given transcervically to 20 heifers. Three

mg of PGF_2 alone was given via the same route to another group of 20 heifers. In the group receiving the SC21009 implants plus $\text{PGF}_{2\alpha}$ 18 of 20 were in estrus and 12 conceived to first service. In the $\text{PGF}_{2\alpha}$ group only 14 of 20 were in estrus over a 5-day period after treatment and 7 conceived to the first service breeding.

Injectable progesterone treatment plus a prostaglandin F analogue (ICI 80, 996) were used by Van Niekerk et al. (1974). They injected 11 cows and 5 heifers with 50 mg progesterone on day 1, 100 mg of progesterone on day 3 and 500 ug $\text{PGF}_{2\alpha}$ analogue (ICI 80, 996) on day 5 followed 12 hr later by 1, 000 i.u. PMSG. The animals were inseminated twice, the first time at the onset of estrus and a second time 12 hr later. Results were 8 of the 16 conceived first service and 3 of the nonresponders were found to be sterile.

Binder et al. (1974) synthesized a series of 16-aryloxy-prostaglandins by slightly altering the chemical structure of prostaglandins. Several of these were found to be many times more potent than $\text{PGF}_{2\alpha}$ in luteolytic activity without being correspondingly more toxic (Dukes, Russell and Walpole, 1974).

Tervit et al. (1973) studied ICI 79,939 and found it to be luteolytic in heifers when given in single IM doses of 1 mg or less between days 5 and 16 of the cycle.

Schmidt et al. (1975) used 0.5 mg of the prostaglandin analogue ICI 80996 for estrous cycle synchronization in cattle. The analogue

was administered IM twice at 11 day intervals. All cattle were inseminated 72 hr after the second treatment without regard for estrus. At 4 locations, 170 animals were treated and first service conception rates ranged from 51 to 67% and in 80 untreated controls 58 to 77%.

Cooper (1974) found that two 500 ug doses IM of ICI 80996, 10 to 12 days apart were successful in synchronizing estrus in Holstein heifers. One hundred-seventy-one of 175 treated exhibited estrus 48 to 96 hr after the second injection. It was also revealed that first service conception was exactly the same in both the treated and control groups.

The ideal estrus synchronization system for cattle would feature appointment breeding at a predetermined time. This would eliminate the need for estrus detection thus an economic saving to the producer. Graves et al. (1975) injected 15 cows between days 9 and 14 of the estrous cycle with 8 mg $\text{PGF}_{2\alpha}$ and 4 mg $\text{PGF}_{2\alpha}$ 24 hr later. This was followed by 250 mg GN-RH 60 hr after the first $\text{PGF}_{2\alpha}$ injection. Results showed that ovulation time from GN-RH was 31.8 ± 1.3 hr. In a second experiment 21 cows were divided into two groups with 11 cows in group 1 and 10 cows in group 2. Group 1 received 6 mg SC 21009 implants on day 1 followed by 10 mg $\text{PGF}_{2\alpha}$ on day 6. An additional 5 mg of $\text{PGF}_{2\alpha}$ was administered at implant removal on day 7. Group 1 cows exhibited estrus 63.1 ± 6.4 hr after implant removal, and ovulation occurred 31.0 ± 1.2 hr after beginning of estrus or 94 ± 7 hr after implant

removal. Group 2 treatment was similar to group 1 except that 125 ug of GN-RH was administered 30 hr after the second $\text{PGF}_{2\alpha}$ injection. Ovulation time from GN-RH was 33 ± 1 hr. It was concluded that GN-RH is effective in reducing variation in ovulation time.

Reeves et al. (1975) randomly divided 60 mature lactating cows into 4 treatment groups. These were a saline, a $\text{PGF}_{2\alpha}$ plus saline, a saline plus LH-RH or a $\text{PGF}_{2\alpha}$ plus LH-RH group. All cows had exhibited at least 1 estrus prior to the experiment. Thirty mg of $\text{PGF}_{2\alpha}$ or equal volumes of saline were used IM at 11 day intervals. LH-RH was administered in 2 mg doses 48 hr after $\text{PGF}_{2\alpha}$ treatments. Breeding took place in cows that received $\text{PGF}_{2\alpha}$ 72 hr after the second $\text{PGF}_{2\alpha}$ injection regardless of estrus. Cows pretreated with saline were bred 24 hr after first signs of estrus. Percent of cows calving (conceived first service AI) was 40, 47, 47, 53% for the saline, $\text{PGF}_{2\alpha}$ plus saline, saline plus LH-RH and the $\text{PGF}_{2\alpha}$ plus LH-RH groups, respectively. It was concluded that cows which were bred at a predetermined time (pretreated with $\text{PGF}_{2\alpha}$) had comparable fertility to the saline pretreated controls.

Kinkie et al. (1976) randomly divided 68 cycling heifers into 5 groups. Groups 1 through 4 were given 2 injections IM of $\text{PGF}_{2\alpha}$ -THAM salt 11 days apart. Of these, groups 1 and 3 received 100 ug IM of GN-RH 60 hr after the second $\text{PGF}_{2\alpha}$ treatment. Groups 1 and 2 were

inseminated twice (at 72 and 96 hr) while groups 3 and 4 were inseminated once (at 80 hr) after the second injection of $\text{PGF}_{2\alpha}$. The controls (group 5) were bred 12 hr after detected in estrus. The first service conception rates for all heifers bred and those showing estrus were 21 and 32% for the GN-RH treated groups and 36 and 48% for the groups not receiving GN-RH, respectively. Differences in conception rates between the treated heifers bred AI for 25 days (63%) and the control heifers (66%) bred AI for 38 days were not significant.

CHAPTER 3

MATERIALS AND METHODS

Breeding studies were conducted at the Montana State Prison Ranch utilizing prostaglandin $F_{2\alpha}$ as an estrus synchronizing agent in beef cattle in the Fall 1974, Spring 1975 and Fall 1975 breeding seasons. Seven groups of cattle were utilized which consisted of: group 1, Fall 1974 bred virgin heifers, $n=92$; group 2, Fall 1974 bred early calving lactating cows, $n=148$; group 3, Fall 1974 bred late calving lactating cows, $n=85$; group 4, Spring 1975 bred 14 mo. virgin heifers, $n=87$; group 5, Spring 1975 bred 20 mo. virgin heifers, $n=153$; group 6, Spring 1975 bred spring calved lactating cows, $n=345$ and group 7, Fall 1975 bred fall calved lactating cows, $n=324$. Cattle in groups 1, 4 and 5 were straight and crossbred beef heifers. Cattle in group 2 were cows from the first half of the Fall 1974 calving season and group 3 were from the second half of the Fall 1974 calving season. Cattle in groups 2, 3, 6 and 7 consisted of straight and crossbred beef cows with calves at side.

Within each group, cattle were randomly divided into either the $PGF_{2\alpha}$ or conventional AI breeding system.

A format for the $PGF_{2\alpha}$ and conventional AI breeding systems is depicted in figure 3. Artificial insemination (AI) was used for 30 days group 1, 28 days group 2 and 22 days for group 3. In groups 4, 5, 6 and 7, AI was used for 25 days. In all groups for both years a

20-day natural breeding period followed. The first AI of all heifers (groups 1, 4 and 5) and crossbred cows (groups 2, 3, 6 and 7) was with homozygous Black Angus semen, while the first AI of the predominantly Hereford cows (groups 2, 3, 6 and 7) was with Hereford semen. All cattle with an estrous cycle of less than 15 days were bred with semen from a Red Angus bull on the second breeding to determine which breeding resulted in conception. The study was conducted during the months of October through December of 1974 and 1975, and June and July 1975.

Detection of estrus was continuous from pre-dawn until dark. Cattle observed in estrus from pre-dawn until 9 a.m. were bred between 5 and 6 p.m. that day while those observed in estrus from 9 a.m. until dark were bred between 5 and 6 a.m. the next day. Detection of estrus started on day⁻¹/₂ and AI started in the a.m. of day 0 in each trial. In the afternoon of day 4 the cattle in the PGF_{2α} breeding system which had not been detected in estrus prior to 9 a.m. on day 4 were injected (IM) with 33.5 mg of PGF_{2α} (THAM salt). Cattle responding to the PGF_{2α} treatment with behavioral estrus were bred in accordance with the general estrus and breeding scheme. Those not detected in estrus by 72 hr postinjection in the fall bred 1974 (groups 1, 2 and 3) were bred and recorded as nonestrus animals. In all 1975 breedings (groups 4, 5, 6 and 7) those cattle not detected in estrus by 80 hr post-injection were bred and recorded as nonestrus animals. At the time of 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 $\text{PGF}_{2\alpha}$ immediately after insemination and the remaining half served as the control. Throughout both years of the study, the $\text{PGF}_{2\alpha}$ and conventional breeding systems were confined in the same pastures.

Conception data for Chapter 4 was determined by rectal palpation at 63 days group 1, 53 days group 2 and 53 days group 3, after the end of the breeding season. Conception data for Chapter 5 was determined by rectal palpation at 83, 83, 62 and 43 days after the end of the breeding season for groups 4, 5, 6 and 7, respectively.

A calculated day of conception was determined based on calving results for Chapter 6. AI bred cows were determined by subtracting gestation lengths of 285 and 279 days for Hereford and Angus sired calves, respectively, from the actual calving date (Clegg, 1959). If the calculated conception date fell within ± 10 days of either the first or second AI breeding date, the corresponding AI breeding date was used as the actual conception date, however, if the calculated conception date was more than 10 days past the last AI breeding date, 20 days (one cycle) was added to the last AI breeding date to determine the approximate natural service conception date. Where it was difficult to determine the actual conception date by the previous guidelines, birth weight and sire breed of the calf were incorporated into the final decision. The approximate conception date for cows with no AI breeding information was calculated by subtracting 285 days from the actual calving date.

Comparisons were made between the $\text{PGF}_{2\alpha}$ and conventional breeding systems and combined animals. The cattle receiving $\text{PGF}_{2\alpha}$ within the PGF_{α} breeding system were also compared to the conventional breeding system. A definition of the following parameters are depicted on the respective tables for total pregnancy rate (tables 1, 9 and 17), total AI pregnancy rate (tables 2, 10 and 18), AI first service pregnancy rate (tables 3, 11 and 19), AI first service conception rate when bred to an observed estrus (tables 4, 12 and 20), and AI first service conception rate when bred nonestrus and received $\text{PGF}_{2\alpha}$ (tables 5, 13 and 21). In Chapter's 5 and 6, the effect of the second injection of $\text{PGF}_{2\alpha}$ administered at the 80 hr nonestrus breeding is assessed. The preceding parameters in addition to the percent pregnant the first 10 days of the AI breeding season were analyzed by two-way chi square. The average day of conception was analyzed by analysis of variance one-way classification. Chapter 6 contains histograms which show the days postpartum of the cows receiving $\text{PGF}_{2\alpha}$ at the date of injection. The AI first service pregnancy rate of cows bred to observed estrus and AI first service pregnancy rate of cows bred nonestrus were evaluated in relation to the days postpartum.

Day of breeding season	PGF _{2α} breeding system	Conventional breeding system
½	Start of detection of estrus	Start of detection of estrus
0*	Start AI	Start AI
1		
2		
3		
4	Cows not bred by day 4 are injected with postaglandin	
5	Continue AI	
6		
7	72 hr for the 1974 breeding (groups 1,2 and 3) and 80 hr for the 1975 breeding (groups 4,5,6 and 7) post-prostaglandin injection, bred all cows which have not been in estrus	
8**	Continue AI	
Additional 20 days	Cleanup bulls	Cleanup bulls

* Breeding seasons began on 10-31, 11-10 and 11-16 for groups 1, 2 and 3 bred fall 1974 and 11-10 group 7 bred fall 1975. For groups 4, 5 and 6 bred spring 1975 the breeding seasons began 6-10, 6-10 and 7-3, respectively.

**Total AI periods were 30, 28 and 22 days for groups 1, 2 and 3 bred fall 1974, respectively, and 25 days for groups 4, 5, 6 and 7 bred in 1975.

Figure 3. Format for the PGF_{2α} and conventional AI breeding systems.

CHAPTER 4

RESULTS AND DISCUSSION OF THE FALL 1974 BREEDING SEASON BASED ON PREGNANCY TEST RESULTS

Total pregnancy rates for the $\text{PGF}_{2\alpha}$ system and those receiving $\text{PGF}_{2\alpha}$ were 86 and 85, 85 and 84 and 84 and 81% for groups 1, 2 and 3, respectively, (table 1). Total pregnancy rates for the conventional system were 70, 86 and 85% for groups 1, 2 and 3, respectively. No statistical differences were found in total pregnancy rates between groups or treatments within groups.

Total AI pregnancy rates were 65, 54 and 37% and 62, 56 and 31% for the $\text{PGF}_{2\alpha}$ system and for those actually receiving $\text{PGF}_{2\alpha}$ for groups 1, 2 and 3, respectively (table 2). In the conventional system, the rates were 51, 45 and 28% for groups 1, 2 and 3, respectively. In the combined analysis, the AI pregnancy rate in both the $\text{PGF}_{2\alpha}$ system (54%) and those receiving $\text{PGF}_{2\alpha}$ (56%) ($P=.04$ and $.02$, respectively) was greater than the conventional system (42%) which demonstrated the ability of a single injection PGF_2 system to improve AI pregnancy rates under range conditions.

The AI first service pregnancy rates were 39, 37 and 34% and 30, 38 and 27% for the $\text{PGF}_{2\alpha}$ system and those actually receiving $\text{PGF}_{2\alpha}$ for groups 1, 2 and 3, respectively (table 3). There were no significant differences when compared to conventional system rates of 47, 43 and 28% for groups 1, 2 and 3, respectively. These data are consistent

with the findings of Lauderdale et al. 1974, King and Robertson 1974, Hafs et al. 1974, Roche, 1974 in which no significant differences in fertility due to use of PGF_{2α} THAM-salt was found.

AI first service conception rates when bred to an observed estrus in the PGF_{2α} system and for those receiving PGF_{2α} were 62, 51 and 43% and 55, 54 and 45% for groups 1, 2 and 3, respectively (table 4). The AI first service conception rates in the conventional system were 65, 54 and 57% for groups 1, 2 and 3, respectively. There were no significant differences in conception rates between the PGF_{2α} system (53%) and the conventional system (57%).

The AI first service conception rates for those cattle bred 72 hr post-PGF_{2α} injection without an observed estrus (by appointment) were 5, 27 and 18% for groups 1, 2 and 3, respectively. No significant differences were found between groups.

The total percent (combined analysis) of cattle detected in estrus during the AI breeding period was 74, 66 and 68% for the PGF_{2α} system, those receiving PGF_{2α} and conventional system, respectively (table 6). There were no significant differences between treatments.

These results clearly demonstrate that there was no difference in total fertility when using a single injection PGF_{2α} system compared to a conventional system under range beef cattle management conditions. There was a trend in these data for the total AI pregnancy rate to be greater ($P=.04$) in the PGF_{2α} system. The fact that the PGF_{2α} system resulted in twice (38 vs 19%, $P=.0004$) the number of cattle pregnant

in the first 10 days of the AI breeding season would account for the desirable trend to move the average day of conception to earlier in the breeding season (tables 7 and 8). These results combined with minimal handling of cattle demonstrated that the single injection $\text{PGF}_{2\alpha}$ system is feasible under range beef cattle management conditions.

Summary

A study was conducted using 92 virgin heifers (group 1), 148 early calving cows (group 2) and 85 late calving cows (group 3), and animals in each group were randomly assigned to a $\text{PGF}_{2\alpha}$ system or a conventional system. The AI season was 30 days (group 1), 28 days (group 2) and 22 days (group 3), each followed by a 20-day natural breeding season. Detection of estrus was continuous during daylight hr and cattle were inseminated approximately 12 hr after detection in both systems. Cattle in the $\text{PGF}_{2\alpha}$ system were observed for estrus and bred from day 0 to 4 at which time the remaining cattle were injected IM with 33.5 mg $\text{PGF}_{2\alpha}$ THAM-salt. Cattle observed in estrus from time of injection until 72 hr post-injection all $\text{PGF}_{2\alpha}$ treated cows that had not been observed in estrus were inseminated. Gestation ranged from 112 to 63, 102 to 53 and 96 to 53 days at time of pregnancy diagnosis in groups 1, 2 and 3, respectively. Total pregnancy rate for the $\text{PGF}_{2\alpha}$ system was equal to control. Total AI pregnancy rate evinced significant differences ($P=.04$) between the $\text{PGF}_{2\alpha}$ system and conventional system

in the combined analysis, indicating higher fertility in the $\text{PGF}_{2\alpha}$ system. The percent of cattle conceiving the first 10 days of the AI season in the $\text{PGF}_{2\alpha}$ system combined analysis was significantly greater ($P=.0004$) than in the combined conventional system. This would account for the trend to move the average day of conception towards the beginning of the breeding season in the single injection $\text{PGF}_{2\alpha}$ system.

TABLE 1. *TOTAL PREGNANCY RATE OF A PGF^{2α} BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)

Group	Treatment		
	PGF ^{2α} system	Receiyng PGF ^{2α}	Conventional system
Fall bred heifers (group 1)	86% $\frac{42}{49}$	85% $\frac{33}{39}$	70% $\frac{30}{43}$
Fall bred early calving cows (group 2)	85% $\frac{58}{68}$	84% $\frac{46}{55}$	86% $\frac{69}{80}$
Fall bred late calving cows (group 3)	84% $\frac{32}{38}$	81% $\frac{21}{26}$	85% $\frac{40}{47}$
Fall bred cows combined (groups 2 and 3)	85% $\frac{90}{106}$	83% $\frac{67}{81}$	86% $\frac{109}{127}$
Combined analysis	85% $\frac{132}{155}$	83% $\frac{99}{120}$	82% $\frac{139}{170}$

*Total pregnant
Total in group

TABLE 2. *TOTAL AI PREGNANCY RATE OF A PGF²_α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)

Group	Treatment		
	PGF ² _α system	Receiving PGF ² _α	Conventional system
Fall bred heifers (group 1)	65% $\frac{32}{49}$	62% $\frac{25}{40}$	51% $\frac{22}{43}$
Fall bred early calving cows (group 2)	54% $\frac{37}{68}$	56% $\frac{31}{55}$	45% $\frac{36}{80}$
Fall bred late calving cows (group 3)	37% $\frac{14}{38}$	31% $\frac{8}{26}$	28% $\frac{13}{47}$
Fall bred cows combined	48% $\frac{51}{106}$	48% $\frac{39}{81}$	39% $\frac{49}{127}$
Combined analysis	54% $\frac{83^a}{155}$	56% $\frac{64^b}{115}$	42% $\frac{71^c}{170}$

a,c P=.0413

b,c P=.0272

* $\frac{\text{Total AI pregnant}}{\text{Total in group}}$

TABLE 3. *AI FIRST SERVICE PREGNANCY RATE OF A PGF²_α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)

Group	PGF ² _α system	Treatment		Conventional system
		Receiving PGF ² _α		
Fall bred heifers (group 1)	38% $\frac{19}{49}$	30% $\frac{12}{40}$	47% $\frac{20}{43}$	
Fall bred early calving cows (group 2)	37% $\frac{25}{68}$	38% $\frac{21}{55}$	43% $\frac{34}{80}$	
Fall bred late calving cows (group 3)	34% $\frac{13}{38}$	27% $\frac{7}{26}$	28% $\frac{13}{47}$	
Fall bred cows combined (groups 2 and 3)	36% $\frac{38}{106}$	35% $\frac{28}{81}$	37% $\frac{47}{127}$	
Combined analysis	37% $\frac{57}{155}$	33% $\frac{40}{121}$	39% $\frac{67}{170}$	

*AI 1st service pregnant
Total group

TABLE 4. *AI FIRST SERVICE CONCEPTION RATE WHEN BRED TO AN OBSERVED ESTRUS IN A PGF²_α BREEDING SYSTEM COMPARED TO A CONVENTIONAL SYSTEM (ALL 1974 BREEDING)

Group	Treatment		
	PGF ² _α system	Receiving PGF ² _α	Conventional system
Fall bred heifers (group 1)	62% $\frac{18}{29}$	55% $\frac{11}{20}$	65% $\frac{20}{31}$
Fall bred early calving cows (group 2)	51% $\frac{20}{39}$	54% $\frac{14}{26}$	54% $\frac{34}{63}$
Fall bred late calving cows (group 3)	43% $\frac{10}{23}$	45% $\frac{4}{9}$	57% $\frac{13}{23}$
Fall bred cows combined (groups 2 and 3)	48% $\frac{30}{62}$	51% $\frac{18}{35}$	55% $\frac{47}{86}$
Combined analysis	53% $\frac{48}{91}$	53% $\frac{29}{55}$	57% $\frac{67}{117}$

* 1st service pregnant

Total group minus nonestrus cattle

TABLE 5. *AI FIRST SERVICE CONCEPTION RATE WHEN BRED NONESTRUS AND RECEIVED PGF²_α (ALL 1974 BREEDING)

Group	<u>Treatment</u> <u>Receiving</u> PGF ² _α
Fall bred heifers (group 1)	5% $\frac{1}{22}$
Fall bred early calving cows (group 2)	27% $\frac{8}{30}$
Fall bred late calving cows (group 2)	18% $\frac{3}{17}$
Fall bred cows combined (groups 2 and 3)	23% $\frac{11}{47}$
Combined analysis	17% $\frac{12}{69}$

* Pregnant 1st service AI
Received PGF²_α and bred nonestrus

TABLE 6. INCIDENCE OF FIRST ESTRUS IN A PGF²_α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)

Group	Parameter									
	Incidence of first estrus in system					Incidence of first estrus by 72 hr post-PGF ² _α				
	Treatment					Total receiving PGF ² _α not showing estrus by 72 hr but returned to estrus at later date				
	PGF ² _α system		Receiving PGF ² _α		Conventional system		Receiving PGF ² _α		Receiving PGF ² _α	
Fall bred heifers (group 1)	83%	$\frac{43}{52}$	78%	$\frac{33}{42}$	68%	$\frac{36}{53}$	48%	$\frac{20}{42}$	59%	$\frac{13}{22}$
Fall bred early cows (group 2)	74%	$\frac{51}{69}$	68%	$\frac{38}{56}$	79%	$\frac{63}{80}$	46%	$\frac{26}{56}$	40%	$\frac{12}{30}$
Fall bred late cows (group 3)	61%	$\frac{23}{38}$	42%	$\frac{11}{26}$	50%	$\frac{24}{48}$	35%	$\frac{9}{26}$	12%	$\frac{2}{17}$
Lactating cows (group 2 & 3)	69%	$\frac{74}{107}$	65%	$\frac{49}{76}$	68%	$\frac{87}{128}$	43%	$\frac{35}{82}$	30%	$\frac{14}{47}$
Combined analysis	74%	$\frac{117}{159}$	66%	$\frac{82}{124}$	68%	$\frac{123}{181}$	44%	$\frac{55}{124}$	39%	$\frac{27}{69}$

TABLE 7. PERCENT OF BEEF CATTLE PREGNANT THE FIRST TEN DAYS OF THE AI BREEDING SEASON WITH ONE AI SERVICE IN A PGF_{2α} BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 BREEDING)

Group	PGF _{2α} system	Conventional system
Heifers (group 1)	39% $\frac{19^a}{49}$	27% $\frac{5^b}{43}$
Early cows (group 2)	40% $\frac{27^c}{68}$	26% $\frac{21^d}{80}$
Late cows (group 3)	34% $\frac{13^e}{38}$	13% $\frac{6^f}{47}$
Combined analysis	38% $\frac{59^g}{155}$	19% $\frac{32^h}{170}$

a,b P=.007

c,d P=.11

e,f P=.03

g,h P=.0004

TABLE 8. THE AVERAGE DAY OF CONCEPTION IN A PGF_{2α} BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (AI AND SUBSEQUENT NATURAL BREEDING SEASON INCLUDED, ALL 1974 BREEDING)

Group	n	PGF _{2α} system day	n	Conventional system day
Heifers (group 1)	43	19	30	21
Early cows (group 2)	59	24	68	26
Late cows (group 3)	32	19	39	27
Lactating cows (groups 2 & 3)	91	22 ^a	107	26 ^b
Combined analysis	134	21 ^c	137	25 ^d

a,b P<.05.

c,d P<.05.

CHAPTER 5

RESULTS AND DISCUSSION OF THE SPRING AND FALL 1975 BREEDING SEASONS BASED ON PREGNANCY TEST RESULTS

Total pregnancy rates for the PGF_{2α} system and those actually receiving PGF_{2α} were 63, 93, 85 and 83% and 59, 92, 81 and 80% for groups 4, 5, 6 and 7, respectively (table 9). Total pregnancy rates for the conventional system were 64, 89, 72 and 81% for groups 4, 5, 6 and 7, respectively. Significant differences were found between the PGF_{2α} system and the conventional system in group 6, revealing a higher total pregnancy rate in the PGF_{2α} system (85%, $P=.0055$) and those receiving PGF_{2α} (81%, $P=.0511$), than for the conventional system (72%). In the combined analysis (groups 4, 5, 6 and 7) for the PGF_{2α} system, the total pregnancy rate (83%) was greater ($P=.0181$) than the total pregnancy rate (77%) for the conventional system.

Total AI pregnancy rates were 51, 77, 46 and 49% and 44, 73, 46 and 46% for the PGF_{2α} system and for those actually receiving PGF_{2α} for groups 4, 5, 6 and 7, respectively (table 10). In the conventional system, the rates were 27, 73, 36 and 36% for groups 4, 5, 6 and 7, respectively. The AI pregnancy rates for group 4 (51%) and group 7 (49%) for the PGF_{2α} system were greater ($P=.0366$ and $.0288$, respectively) than the AI pregnancy rate (27 and 35%, respectively) for the conventional systems. In the combined analysis, the increased AI pregnancy rate in the PGF_{2α} system (52%, $P=.0015$) over the conventional system (41%), demonstrated the ability of a PGF_{2α} breeding

system to improve AI pregnancy rates under range beef production conditions.

The AI first service pregnancy rates were 44, 71, 42 and 42% and 41, 66, 41 and 41% for the $\text{PGF}_{2\alpha}$ system and those actually receiving $\text{PGF}_{2\alpha}$ for groups 4, 5, 6 and 7, respectively (table 11). In the conventional system, the rates were 23, 59, 35 and 35% for groups 4, 5, 6 and 7, respectively. Significant differences were found in group 4, evincing a higher AI first service pregnancy rate in the $\text{PGF}_{2\alpha}$ system (44%, $P=.0548$) than for the conventional system (23%).

In the combined analysis the increased AI first service pregnancy rate in the $\text{PGF}_{2\alpha}$ system (47%, $P=0090$) over the conventional system (38%) is not consistent with the findings of other researchers.

Lauderdale et al. (1974), King and Robertson (1974), Hafs et al. (1974), Roche (1974), Welch et al. (1975) found no significant difference in fertility due to the use of $\text{PGF}_{2\alpha}$ when compared to the conventional system. The higher pregnancy rates seen in the $\text{PGF}_{2\alpha}$ system in this experiment could be explained by the fact that within the limited breeding season (45 days) the cattle in the $\text{PGF}_{2\alpha}$ system are afforded the opportunity to cycle three times rather than two times which is the case for the majority of the cattle in the conventional system.

AI first service conception rates of animals bred to an observed estrus in the $\text{PGF}_{2\alpha}$ system and for those receiving $\text{PGF}_{2\alpha}$ were 69, 78,

57 and 54% and 56, 73, 66 and 48% for groups 4, 5, 6 and 7, respectively (table 12). The AI first service conception rates in the conventional system were 35, 72, 42 and 58% for groups 4, 5, 6 and 7, respectively. In group 6 and the AI first service conception rates of cows bred to an observed estrus were greater for PGF_{2α} system (57%, P=0.435) and those receiving PGF_{2α} (66%, P=.0041) than for the conventional system (42%). In the combined analysis the AI pregnancy rate in both the PGF_{2α} system (62%) and those receiving PGF_{2α} (61%) was greater (P=.0160) and .0516, respectively) than the conventional system (52%).

The AI first service conception rates for those cattle bred 80 hr after the first PGF_{2α} injection without an observed estrus were 35, 52, 25 and 29% for groups 4, 5, 6 and 7, respectively.

Estrus was exhibited by 25% (injected) and 25% (control) of the animals (combined analysis) in the experiment involving the effect of the second injection of PGF_{2α} (table 14). Pregnancy rates were 66% (injected) and 61% (control) and were not significantly different. This indicates no adverse or beneficial effect on fertility resulted from the second injection.

Results clearly demonstrate that there was increased fertility when using a PGF_{2α} system compared to a conventional system under range beef cattle management conditions. There was a convincing trend in these data for the total pregnancy rate and total AI pregnancy rate

to be greater ($P=.0181$ and $.0015$, respectively) in the $\text{PGF}_{2\alpha}$ system reflecting the advantage held by the animals in the PGF_2 system to cycle an additional time during the limits of the breeding season. The $\text{PGF}_{2\alpha}$ system resulted in more than twice (48 vs 20%, $P<.0001$) the number of cattle pregnant in the first 10 days of the AI breeding season. This apparently accounted for the average conception date being seven days earlier for the $\text{PGF}_{2\alpha}$ system compared to the conventional system (tables 15 and 16). These results combined with minimal handling of cattle demonstrated that the $\text{PGF}_{2\alpha}$ breeding system is feasible under range beef cattle management conditions.

Summary

A study was conducted using 87 14-month-old virgin heifers (group 4), 153 20-month-old virgin heifers (group 5), 345 spring calving cows (group 6) and 324 fall calving cows (group 7) and animals in each group were randomly assigned to a $\text{PGF}_{2\alpha}$ system or a conventional breeding system.

The AI season was 25 days for all groups, each followed by a 20-day natural breeding season. Detection of estrus was continuous during daylight hours and cattle were inseminated approximately 12 hr after detection in both systems. Cattle in the $\text{PGF}_{2\alpha}$ system not observed in estrus by day 3 were injected (IM) with 33.5 mg PGF_2 THAM-salt. Cattle observed in estrus from time of injection until 80

hr after the first $\text{PGF}_{2\alpha}$ injection were bred 12 hr after being detected in estrus. At 84 hr after the first injection all $\text{PGF}_{2\alpha}$ treated cows that had not been observed in estrus were inseminated. Immediately after the nonestrus breeding, half of the cattle in this group were given a second injection of 33.5 mg of $\text{PGF}_{2\alpha}$ THAM-salt, and the remaining half served as the control. Days pregnant ranged from 128 to 83, 128 to 83, 107 to 62 and 89 to 43 days at time of pregnancy diagnosis in groups 4, 5, 6 and 7, respectively. Total pregnancy rate was greater ($P=.0180$) in the $\text{PGF}_{2\alpha}$ system (83%) than in the conventional system (77%). The $\text{PGF}_{2\alpha}$ system increased the total AI pregnancy rate (52% vs 41%, $P=.0015$) when compared to the conventional system. Results demonstrated that there was no adverse or beneficial effect on fertility from the second injection of $\text{PGF}_{2\alpha}$. The percent of cattle conceiving the first 10 days of the AI season in the $\text{PGF}_{2\alpha}$ system combined analysis was significantly greater ($P<.0001$) than in the combined conventional system. This resulted in a trend which moved the average day of conception to seven days earlier in the breeding season in the $\text{PGF}_{2\alpha}$ breeding system.

TABLE 9. *TOTAL PREGNANCY RATE OF A PGF²_α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975 BREEDING)

Group	PGF ² _α system	Receiying PGF ² _α	Conventional system
Spring bred 14-mo. heifers (group 4)	63% $\frac{27}{43}$	59% $\frac{23}{39}$	64% $\frac{28}{44}$
Spring bred 20-mo. heifers (group 5)	93% $\frac{70}{75}$	92% $\frac{57}{62}$	89% $\frac{69}{78}$
Spring bred cows (group 6)	$\frac{143^a}{85\% \ 169}$	$\frac{122^b}{81\% \ 150}$	$\frac{126^c}{72\% \ 176}$
Fall bred cows (group 7)	83% $\frac{135}{163}$	80% $\frac{112}{140}$	81% $\frac{130}{161}$
Combined analysis	83% $\frac{375^d}{450}$	80% $\frac{314}{391}$	77% $\frac{353^e}{459}$

a,c P=.005

b,c P=.0511

d,e P=.0181

*Total pregnant
Total in group

TABLE 10. *TOTAL AI PREGNANCY RATE OF A PGF^2_{α} BREEDING SYSTEM
COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975
BREEDING)

Group	Treatment		
	PGF^2_{α} system	Receiving PGF^2_{α}	Conventional system
Spring bred 14-mo. heifers (group 4)	51% $\frac{22^a}{43}$	44% $\frac{17}{39}$	27% $\frac{12^b}{44}$
Spring bred 20-mo. heifers (group 5)	77% $\frac{58}{75}$	73% $\frac{45}{62}$	73% $\frac{57}{78}$
Spring bred cows (group 6)	46% $\frac{78}{169}$	46% $\frac{69}{150}$	36% $\frac{64}{176}$
Fall bred cows (group 7)	49% $\frac{78^c}{163}$	46% $\frac{65}{140}$	36% $\frac{57^d}{161}$
Combined analysis	52% $\frac{236^e}{450}$	48% $\frac{196}{410}$	41% $\frac{190^f}{459}$

a,b P=.0366

c,d P=.0288

e,f P=.0015

* $\frac{\text{Total AI pregnant}}{\text{Total in group}}$

TABLE 11. *AI FIRST SERVICE PREGNANCY RATE OF A PGF² α BREEDING SYSTEM
COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975
BREEDING)

Group	Treatment		
	PGF ² α system	Receiving PGF ² α	Conventional system
Spring bred 14-mo. heifers (group 4)	44% $\frac{19^a}{43}$	41% $\frac{16}{39}$	23% $\frac{10^b}{44}$
Spring bred 20-mo. heifers (group 5)	71% $\frac{53}{75}$	66% $\frac{41}{62}$	59% $\frac{46}{78}$
Spring bred cows (group 6)	42% $\frac{71}{169}$	41% $\frac{62}{150}$	35% $\frac{62}{176}$
Fall bred cows (group 7)	42% $\frac{68}{163}$	41% $\frac{57}{140}$	35% $\frac{57}{161}$
Combined analysis	47% $\frac{211^c}{450}$	44% $\frac{179}{410}$	38% $\frac{175^d}{459}$

a,b P=.0548

c,d P=.0090

* AI 1st service pregnant

Total group

TABLE 12. *AI FIRST SERVICE CONCEPTION RATE WHEN BRED TO AN OBSERVED ESTRUS IN A PGF^{2α} BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975 BREEDING)

Group	Treatment		
	PGF ^{2α} system	Receiving PGF ^{2α}	Conventional system
Spring bred 14-mo. heifers (group 4)	69% $\frac{9}{13}$	56% $\frac{5}{9}$	35% $\frac{10}{29}$
Spring bred 20-mo. heifers (group 5)	78% $\frac{43}{55}$	73% $\frac{30}{41}$	72% $\frac{46}{64}$
Spring bred cows (group 6)	57% $\frac{42^a}{74}$	66% $\frac{35^b}{53}$	42% $\frac{62^c}{149}$
Fall bred cows (group 7)	54% $\frac{45}{83}$	48% $\frac{29}{60}$	58% $\frac{47}{81}$
Combined analysis	62% $\frac{139^e}{225}$	61% $\frac{99^f}{163}$	52% $\frac{165^g}{323}$

a,c P=.0435

b,c P=.0041

e,g P=.0160

f,g P=.0516

* AI 1st service pregnant

Total group minus nonestrus cattle

TABLE 13. *AI FIRST SERVICE CONCEPTION RATE WHEN BRED NONESTRUS AND RECEIVED PGF²_α (ALL 1975 BREEDING)

Group	Treatment	
	Receiving PGF ² _α	
Spring bred 14-mo. heifers (group 4)	35%	$\frac{11}{31}$
Spring bred 20-mo. heifers (group 5)	52%	$\frac{11}{21}$
Spring bred cows (group 6)	25%	$\frac{24}{95}$
Fall bred cows (group 7)	29%	$\frac{23}{79}$
Combined analysis	30%	$\frac{69}{229}$

* AI 1st service prègnant
Received PGF²_α and bred nonestrus

TABLE 14. THE EFFECT OF THE SECOND INJECTION OF $\text{PGF}_{2\alpha}$ AT THE 80 HR NONESTRUS BREEDING ON ESTRUS AND PREGNANCY RATES (ALL 1975 BREEDING)

Group	Received 2nd injection		Control	
	Estrus	Preg. rate	Estrus	Preg. rate
Heifers 14-mo. (group 4)	6% $\frac{1}{17}$	65% $\frac{11}{17}$	13% $\frac{2}{16}$	44% $\frac{7}{16}$
Heifers 20-mo. (group 5)	25% $\frac{3}{12}$	67% $\frac{8}{12}$	27% $\frac{4}{15}$	60% $\frac{9}{15}$
Spring cows (group 6)	36% $\frac{14}{39}$	56% $\frac{22}{39}$	30% $\frac{10}{33}$	55% $\frac{18}{33}$
Fall cows (group 7)	24% $\frac{9}{38}$	76% $\frac{29}{38}$	20% $\frac{8}{40}$	73% $\frac{29}{40}$
Combined analysis	26% $\frac{27}{106}$	66% $\frac{70}{106}$	25% $\frac{26}{104}$	61% $\frac{63}{104}$

TABLE 15. PERCENT OF BEEF CATTLE PREGNANT THE FIRST TEN DAYS OF THE AI BREEDING SEASON WITH ONE AI SERVICE IN A PGF_{2α} BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1975 BREEDING)

Group	PGF _{2α} system	Conventional system
Heifers 14-mo. (group 4)	44% $\frac{19^a}{43}$	7% $\frac{3^b}{44}$
Heifers 20-mo. (group 5)	72% $\frac{54^c}{75}$	41% $\frac{32^d}{78}$
Spring cows (group 6)	45% $\frac{76^e}{169}$	17% $\frac{29^f}{176}$
Fall cows (group 7)	40% $\frac{65^g}{163}$	17% $\frac{27^h}{161}$
Combined analysis	48% $\frac{241^i}{450}$	20% $\frac{91^j}{459}$

a,b P=.0004.

c,d P=.0005.

e,f P<.0001.

g,h P=.0001.

i,j P<.0001.

TABLE 16. THE AVERAGE DAY OF CONCEPTION IN A PGF²_α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (AI AND SUBSEQUENT NATURAL BREEDING SEASON INCLUDED) (ALL 1975 BREEDING)

Group	n	PGF ² _α system day	n	Conventional system day
Heifers 14-mo. (group 4)	27	12 ^a	30	24 ^b
Heifers 20-mo. (group 5)	63	9 ^c	67	17 ^d
Spring cows (group 6)	138	16 ^e	107	20 ^f
Fall cows (group 7)	128	17 ^g	128	24 ^h
Combined analysis	356	14 ⁱ	331	21 ^j

a,b P=.001

c,d P<.001

e,f P=.011

g,h P<.001

i,j P<.001

CHAPTER 6

RESULTS AND DISCUSSION OF THE FALL 1974, SPRING AND FALL 1975 BREEDING SEASONS BASED ON CALVING RESULTS

Total pregnancy rate (table 17) for the $\text{PGF}_{2\alpha}$ breeding system (78%, combined analysis, groups 1 through 7), was significantly higher ($P=.0185$) than the conventional breeding system (72%). The higher total pregnancy rate in the $\text{PGF}_{2\alpha}$ system could be explained by the fact that within the limited breeding season (45 days) the cattle in the $\text{PGF}_{2\alpha}$ system are afforded the opportunity to cycle three times rather than two times which is the case for the majority of the cattle in the conventional system.

Total AI pregnancy rate (table 18) for the $\text{PGF}_{2\alpha}$ breeding system (47%, combined analysis, groups 1 through 7) was significantly greater ($P=.0016$) than the conventional breeding system (39%). These results demonstrate the ability of the $\text{PGF}_{2\alpha}$ breeding system to improve total AI pregnancy rate under range beef production conditions.

AI first service pregnancy rate (table 19) for the $\text{PGF}_{2\alpha}$ breeding system (37%, combined analysis, groups 1 through 7) was not significantly different from the conventional breeding system (36%). These results are consistent with other studies where no significant difference in fertility was observed due to the use of $\text{PGF}_{2\alpha}$ when compared to controls (Lauderdale et al., 1974; King and Robertson, 1974; Hafs et al., 1974; Roche, 1974; Welch et al., 1975).

In the $\text{PGF}_{2\alpha}$ breeding system, all cows were inseminated by the a.m. of day 8 of the breeding season. Under these conditions a large percentage of animals were inseminated at approximately 72 hr (Fall 1974 breeding) or 80 hr (Spring and Fall 1975 breedings) post $\text{PGF}_{2\alpha}$ treatment without being observed in estrus (nonestrus). Assuming that some of the cattle bred nonestrus in the $\text{PGF}_{2\alpha}$ system were either prepubertal heifers or anestrus cows, one would expect the AI first service pregnancy rate in the $\text{PGF}_{2\alpha}$ breeding system to be decreased, however, no significant differences were detected in any group for AI first service pregnancy rate between breeding systems for either the 1974 or 1975 breedings. The fact that AI first service pregnancy rates were not reduced and that in groups 1, 3, 4, 5 and 7 a non-significant trend is indicated toward increased AI first service pregnancy rates (table 19), suggests that the $\text{PGF}_{2\alpha}$ breeding system may enhance AI first service pregnancy rate. An explanation of this observation could be either a direct effect of $\text{PGF}_{2\alpha}$ or differences in the error associated with estrus detection between breeding systems. Errors in estrus detection resulting from either silent or undetected estrus occur in both breeding systems, however, the problem is less severe in the $\text{PGF}_{2\alpha}$ breeding system because all cattle are inseminated by the a.m. of day 8 of the breeding season. Cattle with a $\text{PGF}_{2\alpha}$ induced ovulation accompanied by a silent or undetected estrus have a chance to conceive first service AI while cattle in the

conventional system with silent or undetected estrus do not get inseminated. Therefore, a greater error in estrus detection in the conventional system could reduce the AI first service pregnancy rate and could offset any negative effect from breeding nonestrous cattle in the PGF_{2α} system that were not cycling.

These results unequivocally demonstrate that total pregnancy rate, total AI pregnancy rate and AI first service pregnancy rate in the PGF_{2α} breeding system, are in all cases comparable and in some cases superior to those for the conventional breeding system. In addition, these results demonstrate that estrus synchronization of beef cattle under range conditions can be successfully employed by a single injection of PGF_{2α} administered on the fifth day of breeding without affecting fertility at the first post PGF_{2α} breeding. Early estrus synchronization studies, featuring various progestogen compounds showed decreased AI first service fertility at the first post treatment estrus when compared to nontreated controls (Trimberger and Hansel, 1955; Ulberg and Lindley, 1960; Wiltbank et al., 1965; Dhindsa et al., 1967). More recent studies using the progestogen compound SC21009 (ear implants) in combination with estradiol valerate, in addition to employing a shorter duration progestogen treatment, have found fertility to be comparable to controls (Burrell et al., 1972, Whitman et al., 1972 and Wishart and Young, 1974). Due to the stress related to administration of implants

and handling of the cattle these agents have not been readily accepted for estrus synchronization.

The following analyses were conducted to assess the effect(s) of breeding estrus and nonestrus cattle. The AI first service conception rate of cattle inseminated to an observed estrus (table 20) for the PGF_{2α} breeding system (55%, combined analysis, groups 1 through 7) was comparable with the conventional breeding system (36%). These results demonstrate that fertility of the PGF_{2α} induced estrus is comparable to the naturally occurring estrus of the conventional breeding system.

The AI first service conception rate for cattle inseminated at the nonestrus breeding was 16% in combined analysis (group 1 through 7, table 21). The low conception rate observed at the nonestrus breeding could be attributed to the fact that in this breeding management system, anestrus and infertile cattle were inseminated. In addition, the timing of the nonestrus breeding in relation to when ovulation occurs in these cattle may be a factor contributing to the low conception rate.

Total pregnancy rate (table 24), total AI pregnancy rate (table 25) and AI first service pregnancy rate (table 26) for cattle receiving the second injection of PGF_{2α} and for controls were 73 and 63%, 30 and 18% and 12 and 11%, respectively. These data were not statistically different, however, a nonsignificant trend ($P=.0766$) suggests an increased total AI pregnancy rate for those cattle receiving the

the second PGF₂ α injection (table 25).

In a combined analysis of the first 10 days of the AI breeding season (table 22), the AI pregnancy rates were increased ($P < .0001$) for the PGF₂ α breeding system (41%) over the conventional breeding system (17%).

Figures 4 and 5 depict the percent of the herd pregnant per day throughout the AI breeding season. Of the cattle that conceived during the AI season in the PGF₂ α breeding system, 82% (1974 breeding) and 78% (1975 breedings) had done so by day 10 compared to 54% (1974 breeding) and 38% (1975 breeding) for the conventional system. These results demonstrate the ability of a PGF₂ α breeding system to essentially accomplish in 10 days what is accomplished in 25 days in a conventional breeding system. As a result of a greater number of cattle conceiving early in the breeding season, the average day of conception (table 23) was advanced five days ($P < .001$, combined analysis) for the PGF₂ α breeding system when compared to the conventional breeding system.

Breeding systems utilizing two injections of PGF₂ α necessitates a minimum of at least three handlings of the cattle. A desirable feature of the single injection system of administering PGF₂ α , is that the injection and first insemination can be accomplished with a maximum of two chute runs per cow.

A study of the AI first service pregnancy rate (combined 1974 and 1975 breedings) vs days postpartum at the day of PGF₂ α injection

(figure 6), reveals a trend for pregnancy rate to increase until cattle are 65 days postpartum. At this time, the rate tends to decrease until 75 days postpartum. The AI first service pregnancy rate then increases until approximately 83 days postpartum at which time the rate begins to decline.

The estrus response (combined 1974 and 1975 breedings) of these same cattle reveals a similar increasing trend (figure 7) as the number of days postpartum advances. There are, however, slight decreases in the estrus response again for those cattle that are 69 to 72 days postpartum.

The AI first service pregnancy rate of cattle inseminated to an observed estrus (combined 1974 and 1975 breedings) vs days postpartum at the day of $\text{PGF}_{2\alpha}$ injection (figure 8) suggests that cattle in the range of 69 to 80 days postpartum exhibit a trend for a decreased pregnancy rate. The AI first service pregnancy rate of cattle inseminated nonestrus (combined 1974 and 1975 breedings) vs days postpartum at the day of $\text{PGF}_{2\alpha}$ injection (figure 9) also suggests that cattle in the range of 69 to 76 days postpartum exhibit a trend for a decreased pregnancy rate. A precise explanation of these observations is not available. It may be speculated that the decreased pregnancy rates may be due to an effect of either treatment or lactational stress on the cow. In order to partially explain these results, further study

is required comparing AI first service pregnancy rate vs days postpartum of cattle in the conventional system to those cattle that received PGF_{2α}.

Estrus response of PGF_{2α} treated cattle vs days postpartum on the day of PGF_{2α} injection, AI first service pregnancy rate of PGF_{2α} treated cattle inseminated to observed estrus vs days postpartum on the day of PGF_{2α} injection and AI first service pregnancy rate of PGF_{2α} injection are depicted in appendix figures 1 through 12 for individual groups 1 through 7.

Summary

Breeding studies were conducted at the Montana State Prison Ranch utilizing PGF_{2α} as an estrus synchronizing agent in beef cattle in the Fall 1974 and Spring and Fall 1975 breeding seasons. Seven groups of cattle were utilized which consisted of: group 1, Fall 1974 bred virgin heifers, n=92; group 2, Fall 1974 bred early calving lactating cows, n=148; group 3, Fall 1974 bred late calving lactating cows, n=85; group 4, Spring 1975 bred 14-mo. virgin heifers, n=87; group 5, Spring 1975 bred 20-mo. virgin heifers, n=153; group 6, Spring 1975 bred spring calved lactating cows, n=345 and group 7, Fall 1975 bred Fall calved lactating cows, n=324. Cattle in groups 1, 4 and 5 were straight and crossbred beef heifers. Cattle in groups 2 were cows from the first half of the Fall 1974 calving season and group 3 were from the second half of the Fall 1974 calving season. Cattle in groups 2, 3

6 and 7 consisted of straight and crossbred beef cows with calves at side. Cattle within each group were randomly assigned into either the $\text{PGF}_{2\alpha}$ or conventional AI breeding system. The AI season was 30, 28, 22, 25, 25, 25 and 25 days for groups 1, 2, 3, 4, 5, 6, and 7, respectively, each followed by a 20-day natural breeding season. Detection of estrus was periodic from pre-dawn until dark. Cattle in both systems that were detected in estrus from pre-dawn until 9 a.m. were inseminated at approximately 5 p.m. while those detected from 9 a.m. until dark were inseminated at 5 a.m. the next day. Cattle in the $\text{PGF}_{2\alpha}$ system were observed for estrus and bred from day 0 to 4 at which time remaining cattle in the $\text{PGF}_{2\alpha}$ system were injected IM with 33.5 mg $\text{PGF}_{2\alpha}$ THAM-salt. Cattle observed in estrus from the time of injection until 72 hr post-injection (groups 1, 2 and 3) or 80 hr post-injection (groups 4, 5, 6 and 7) were bred in accordance with the general breeding scheme. At 72 hr post-injection (groups 1, 2 and 3) or 80 hr (groups 4, 5, 6 and 7) all $\text{PGF}_{2\alpha}$ treated cows that had not been observed in estrus were inseminated (nonestrus). Immediately after the nonestrus breeding, half of the cattle in the nonestrus breeding were given a second injection of 33.5 mg of $\text{PGF}_{2\alpha}$ THAM-salt, and the remaining half served as the control. Total pregnancy rate combined analysis (groups 1, 2, 3, 4, 5, 6 and 7) for the $\text{PGF}_{2\alpha}$ system was significantly higher (78 vs 72%, $P=.0185$) than

in the conventional system. Group 6 revealed a higher total pregnancy rate in the PGF_{2α} system (80%, P=0.327) than for the conventional system (70%). The total pregnancy rates for the PGF_{2α} and conventional systems were not significantly different for groups 1, 2, 3, 4 and 5 or 7. In the combined analysis (groups 1 through 7) the total AI pregnancy rate for the PGF_{2α} system was significantly higher (47%, P=0.016) than the conventional system (39%). In group 7 the total AI pregnancy rate for the PGF_{2α} system (40%, P=.0115) and those receiving PGF₂ (38%, P=.0447) was significantly higher than the conventional system (26%). The total AI pregnancy rates were not significantly different for groups 1, 2, 3, 4, 5 and 6. There were no significant differences between systems for AI first service pregnancy rate in any group. The AI first service conception rate when bred to an observed estrus in the PGF_{2α} system was comparable to controls for groups 1, 2, 3, 4, 5 and 7. In group 6 the AI first service conception rate when bred to an observed estrus was higher for the PGF_{2α} system (58%, P=0.130) and for those receiving PGF_{2α} (62%, P=.0073) than in the conventional system (40%). The cattle receiving the second injection of PGF_{2α} at the 80 hr nonestrus breeding (groups 4, 5, 6 and 7) revealed no significant differences in total pregnancy rate, total AI pregnancy rate or AI first service pregnancy rate when compared to controls. In a combined analysis (groups 1 through 7) the number

of cows conceiving the first 10 days of the AI season was greater ($P < .0001$ in the $\text{PGF}_{2\alpha}$ system than in the conventional breeding system. This resulted in the average day of conception being 5 days earlier in the $\text{PGF}_{2\alpha}$ breeding system ($P < .001$, day 17) compared to the conventional system (day 22). A study relating AI first service pregnancy rate vs days postpartum at the day of $\text{PGF}_{2\alpha}$ injection, estrus response of $\text{PGF}_{2\alpha}$ treated cattle vs days postpartum on the day of $\text{PGF}_{2\alpha}$ injection, AI first service pregnancy rate of $\text{PGF}_{2\alpha}$ treated cattle inseminated to observed estrus vs days postpartum on the day of $\text{PGF}_{2\alpha}$ treated cattle inseminated nonestrus vs days postpartum on the day of $\text{PGF}_{2\alpha}$ injection indicated that fertility may be decreased when a cow is approximately 75 days postpartum.

TABLE 17. *TOTAL PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 and 1975 BREEDING)

Group	Treatment		Conventional system
	PGF2 α system	Receiving PGF2 α	
Fall bred heifers (group 1)	76% $\frac{37}{49}$	69% $\frac{27}{39}$	64% $\frac{27}{42}$
Fall bred early calving cows (group 2)	78% $\frac{53}{68}$	75% $\frac{41}{55}$	84% $\frac{66}{79}$
Fall bred late calving cows (group 3)	79% $\frac{30}{38}$	77% $\frac{20}{26}$	76% $\frac{35}{46}$
Spring bred 14-mo. heifers (group 4)	61% $\frac{25}{41}$	61% $\frac{22}{36}$	55% $\frac{24}{44}$
Spring bred 20-mo. heifers (group 5)	87% $\frac{64}{74}$	79% $\frac{48}{61}$	79% $\frac{62}{79}$
Spring bred cows (group 6)	80% $\frac{133^a}{167}$	75% $\frac{110}{147}$	70% $\frac{113^b}{164}$
Fall bred cows (group 7)	76% $\frac{122}{161}$	73% $\frac{102}{140}$	70% $\frac{114}{162}$
Combined analysis	78% $\frac{464^c}{598}$	73% $\frac{370}{504}$	72% $\frac{441^d}{616}$

a,b P=.0327

c,d P=.0185

*Total pregnant
Total in group

TABLE 18. *TOTAL AI PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM
COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974
AND 1975 BREEDING)

Group	PGF2 α		Treatment		Conventional	
	system		Receiving PGF2 α		system	
Faal bred heifers (group 1)	67%	$\frac{33}{49}$	62%	$\frac{24}{39}$	52%	$\frac{22}{42}$
Fall bred early calving cows (group 2)	53%	$\frac{36}{68}$	53%	$\frac{29}{55}$	54%	$\frac{43}{79}$
Fall bred late calving cows (group 3)	42%	$\frac{16}{38}$	31%	$\frac{8}{26}$	37%	$\frac{17}{46}$
Spring bred 14-mo. heifers (group 4)	27%	$\frac{11}{41}$	22%	$\frac{8}{36}$	21%	$\frac{9}{44}$
Spring bred 20-mo. heifers (group 5)	62%	$\frac{46}{74}$	51%	$\frac{31}{61}$	49%	$\frac{39}{79}$
Spring bred cows (group 6)	45%	$\frac{75}{167}$	37%	$\frac{55}{147}$	37%	$\frac{60}{164}$
Fall bred cows (group 7)	40%	$\frac{65^a}{161}$	38%	$\frac{53^b}{140}$	26%	$\frac{43^c}{162}$
Combined analysis	47%	$\frac{282^e}{598}$	41%	$\frac{208}{504}$	38%	$\frac{233^f}{616}$

a,b P=.0115

b,c P=.0447

e,f P=.0016

*Total AI pregnant
Total in group

TABLE 19. *AI FIRST SERVICE PREGNANCY RATE OF A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 AND 1975 BREEDING)

Group	Treatment		
	PGF2 α system	Receiving PGF2 α	Conventional system
Fall bred heifers (group 1)	61% $\frac{30}{49}$	56% $\frac{22}{39}$	50% $\frac{21}{42}$
Fall bred early calving cows (group 2)	35% $\frac{24}{68}$	36% $\frac{20}{55}$	51% $\frac{40}{79}$
Fall bred late calving cows (group 3)	40% $\frac{15}{38}$	27% $\frac{7}{26}$	37% $\frac{17}{46}$
Spring bred 14-mo. heifers (group 4)	27% $\frac{11}{41}$	22% $\frac{8}{36}$	21% $\frac{9}{44}$
Spring bred 20-mo. heifers (group 5)	55% $\frac{41}{74}$	46% $\frac{28}{61}$	48% $\frac{38}{79}$
Spring bred cows (group 6)	32% $\frac{53}{167}$	27% $\frac{40}{147}$	35% $\frac{58}{164}$
Fall bred cows (group 7)	30% $\frac{49}{161}$	27% $\frac{38}{140}$	25% $\frac{41}{162}$
Combined analysis	37% $\frac{223}{598}$	32% $\frac{163}{504}$	36% $\frac{224}{616}$

*AI 1st service pregnant
Total group

TABLE 20. *AI FIRST SERVICE CONCEPTION RATE WHEN BRED TO AN OBSERVED ESTRUS IN A PGF2 α CONVENTIONAL BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (ALL 1974 AND 1975 BREEDING)

Group	PGF2α		Treatment		Conventional
	system		Receiving PGF2α		
Fall bred heifers (group 1)	62%	$\frac{18}{29}$	58%	$\frac{11}{19}$	70% $\frac{21}{30}$
Fall bred early calving cows (group 2)	51%	$\frac{20}{39}$	58%	$\frac{15}{26}$	65% $\frac{40}{62}$
Fall bred late calving cows (group 3)	62%	$\frac{13}{21}$	56%	$\frac{5}{9}$	71% $\frac{17}{24}$
Spring bred 14-mo. heifers (group 4)	54%	$\frac{7}{13}$	44%	$\frac{4}{9}$	24% $\frac{7}{29}$
Spring bred 20-mo. heifers (group 5)	64%	$\frac{35}{55}$	61%	$\frac{25}{41}$	63% $\frac{40}{64}$
Spring bred cows (group 6)	58%	$\frac{43^a}{74}$	62%	$\frac{33^b}{53}$	40% $\frac{59^c}{149}$
Fall bred cows (group 7)	45%	$\frac{37}{83}$	45%	$\frac{27}{60}$	52% $\frac{42}{81}$
Combined analysis	55%	$\frac{173}{314}$	55%	$\frac{120}{217}$	51% $\frac{226}{439}$

a,c P=.0130

b,c P=.0073

*AI 1st service pregnant

Total group minus non-estrus cattle

TABLE 21. *AI FIRST SERVICE CONCEPTION RATE WHEN BRED NON-ESTRUS AND
RECEIVED PGF2 α (ALL 1974 AND 1975 BREEDING)

Group	Treatment Receiving PGF2 α
Fall bred heifers (group 1)	55% $\frac{11}{20}$
Fall bred early calving cows (group 2)	17% $\frac{5}{29}$
Fall bred late calving cows (group 3)	12% $\frac{2}{17}$
Spring bred 14-mo. heifers (group 4)	13% $\frac{4}{32}$
Spring bred 20-mo. heifers (group 5)	25% $\frac{5}{20}$
Spring bred cows (group 6)	9% $\frac{8}{92}$
Fall bred cows (group 7)	14% $\frac{11}{79}$
Combined analysis	16% $\frac{46}{289}$

*Pregnant one service AI
Received PGF2 α and bred non-estrus

TABLE 22. *PERCENT OF BEEF CATTLE PREGNANT THE FIRST TEN DAYS OF THE AI BREEDING SEASON IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL AI BREEDING SYSTEM (ALL 1974 AND 1975 BREEDING)

Group	Treatment	
	PGF2 α system	Conventional system
Fall bred heifers (group 1)	63% $\frac{31^a}{49}$	21% $\frac{9^b}{42}$
Fall bred early calving cows (group 2)	40% $\frac{27}{68}$	29% $\frac{23}{79}$
Fall bred late calving cows (group 3)	42% $\frac{16^c}{38}$	17% $\frac{8^d}{46}$
Spring bred 14-mo. heifers (group 4)	27% $\frac{11^e}{41}$	7% $\frac{3^f}{44}$
Spring bred 20-mo. heifers (group 5)	61% $\frac{45^g}{74}$	18% $\frac{14^h}{79}$
Spring bred cows (group 6)	35% $\frac{58^i}{167}$	15% $\frac{25^j}{164}$
Fall bred cows (group 7)	37% $\frac{59^k}{161}$	14% $\frac{23^l}{162}$
Combined analysis	41% $\frac{247^m}{598}$	17% $\frac{105^n}{616}$

a,b P=.0004

c,d P=.0228

e,f P=.0266

g,h P<.0001

i,j P=.0002

k,l P=.0001

m,n P<.0001

*

TABLE 23. *THE AVERAGE DAY OF CONCEPTION IN A PGF2 α BREEDING SYSTEM COMPARED TO A CONVENTIONAL BREEDING SYSTEM (AI AND SUBSEQUENT NATURAL BREEDING SEASON INCLUDED) (ALL 1974 AND 1975 BREEDING)

Group	n	PGF2 α system day	n	Conventional system Day
Fall bred heifers (group 1)	38	10 ^a	27	15 ^b
Fall bred early calving cows (group 2)	54	19	66	19
Fall bred late calving cows (group 3)	30	16	35	19
Spring bred 14-mo. heifers (group 4)	25	21	24	25
Spring bred 20-mo. heifers (group 5)	64	13 ^c	62	21 ^d
Spring bred cows (group 6)	133	20	113	22
Fall bred cows (group 7)	122	18 ^e	114	25 ^f
Combined analysis	466	17 ^g	441	22 ^h

a,b P=.052

c,d P=.001

e,f P<.001

g,h P<.001

TABLE 24. THE EFFECT OF THE SECOND INJECTION OF PGF_{2α} AT THE 80 HR NON-ESTRUS BREEDING ON TOTAL PREGNANCY RATE (ALL 1975 BREEDING)

Group	Received 2nd injection	Control
Heifers		
14-month (group 4)	63% $\frac{10}{16}$	47% $\frac{7}{15}$
Heifers		
20-month (group 5)	89% $\frac{8}{9}$	73% $\frac{8}{11}$
Spring cows (group 6)	80% $\frac{20}{25}$	67% $\frac{16}{24}$
Fall cows (group 7)	70% $\frac{28}{40}$	63% $\frac{25}{40}$
Combined analysis	73% $\frac{66}{90}$	62% $\frac{56}{90}$

TABLE 25. THE EFFECT OF THE SECOND INJECTION OF PGF_{2α}. AT THE 80 HR NON-ESTRUS BREEDING ON TOTAL AI PREGNANCY RATE (ALL 1975 BREEDING)

Group	Received 2nd injection	Control
Hiefers 14-month (group 4)	13% $\frac{2}{16}$	13% $\frac{2}{15}$
Heifers 20-month (group 5)	44% $\frac{4}{9}$	27% $\frac{3}{11}$
Spring cows (group 6)	28% $\frac{7}{25}$	17% $\frac{4}{24}$
Fall cows (group 7)	35% $\frac{14}{40}$	18% $\frac{7}{40}$
Combined analysis	30% $\frac{27^a}{90}$	18% $\frac{16^b}{90}$

a, b P=.0766

TABLE 26. THE EFFECT OF THE SECOND TREATMENT OF PGF2 α AT THE 80 HR NON-ESTRUS BREEDING ON AI FIRST SERVICE PREGNANCY RATE (ALL 1975 BREEDING)

Group	Received 2nd injection	Control
Heifers 14-month (group 4)	13% $\frac{2}{16}$	13% $\frac{2}{15}$
Heifers 20-month (group 6)	44% $\frac{4}{9}$	9% $\frac{1}{11}$
Spring cows (group 6)	0% $\frac{0}{25}$	4% $\frac{1}{24}$
Fall cows (group 7)	13% $\frac{5}{40}$	15% $\frac{6}{40}$
Combined analysis	12% $\frac{11}{90}$	11% $\frac{10}{90}$

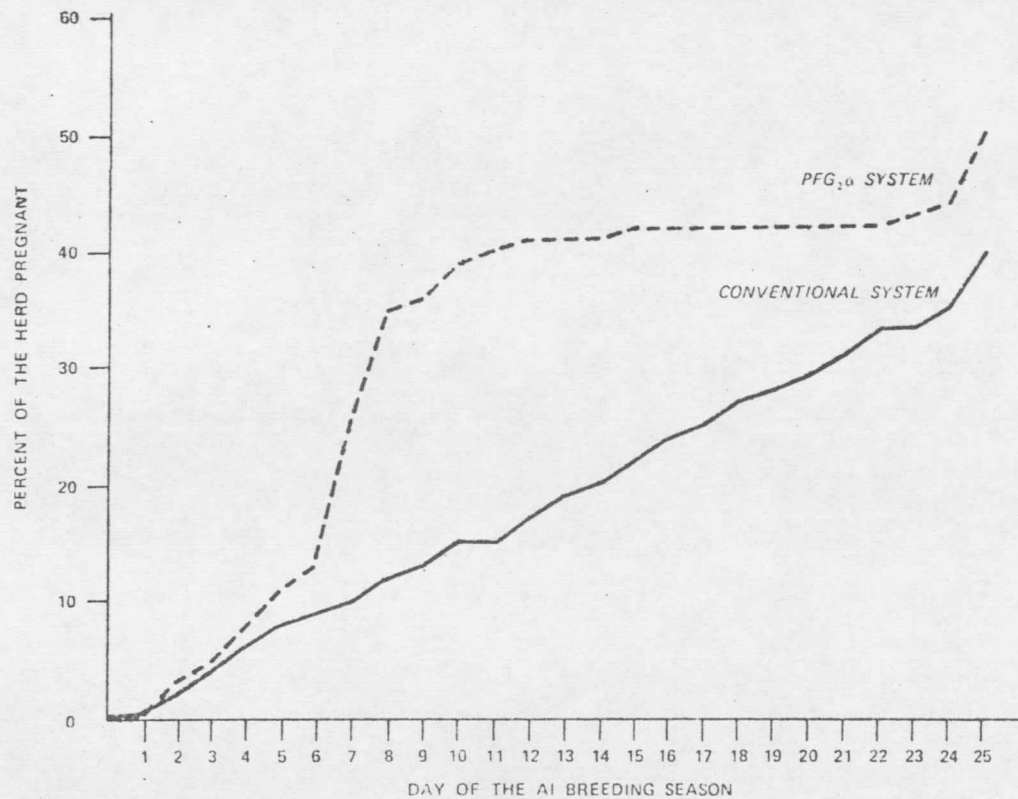


Figure 4. Percent of the herd pregnant per day of the AI season in the PGF₂α and conventional breeding systems for the 1974 (combined analysis).

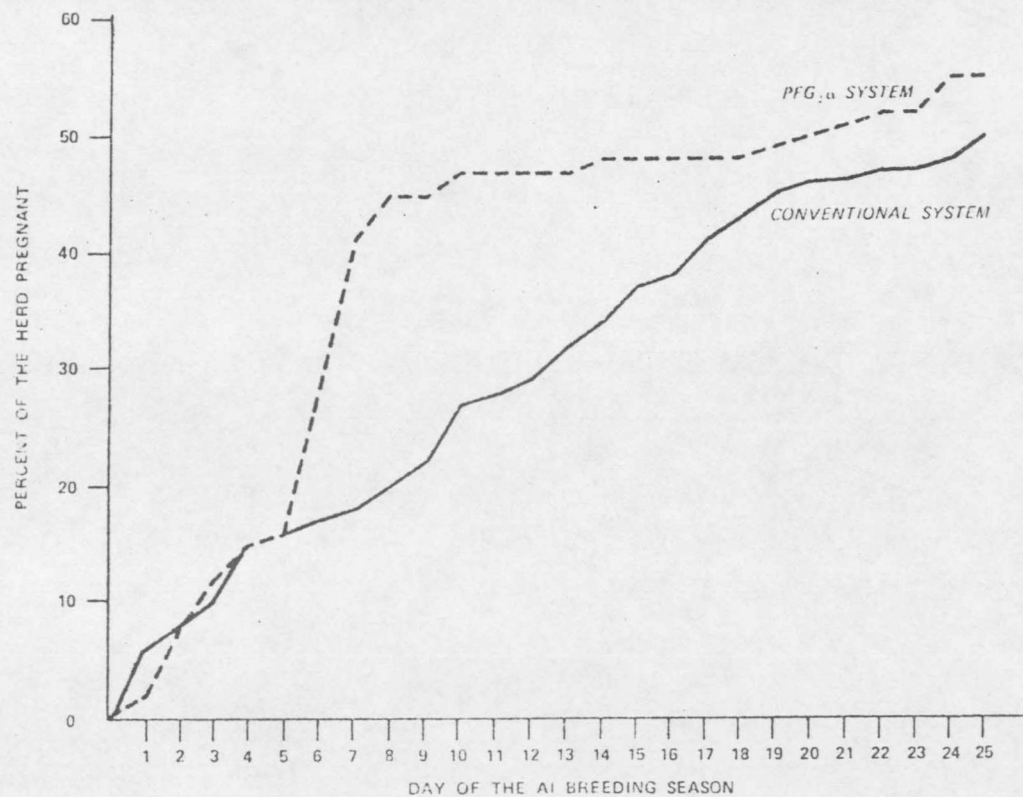


Figure 5. Percent of the herd pregnant per day of the AI season in the PGF₂α and conventional breeding systems for the 1975 (combined analysis).

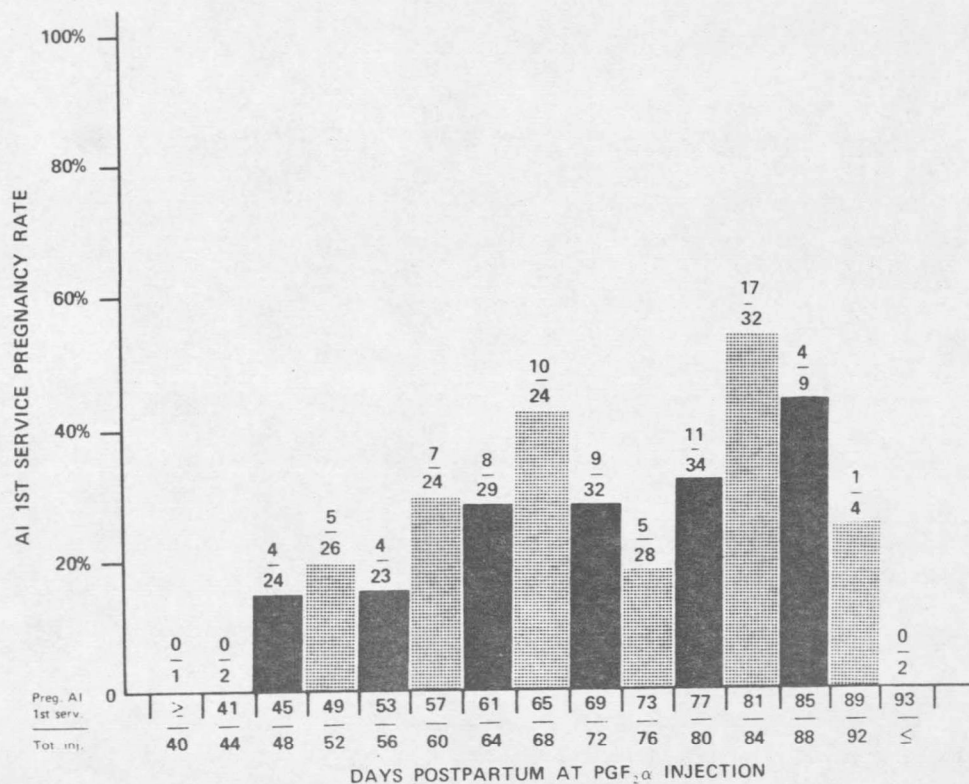


Figure 6. AI 1st service pregnancy rate (cattle inseminated to estrus and non-estrus) vs. days postpartum on the day of PGF₂α injection for mature cows in the 1974 and 1975 breeding seasons (combined analysis).

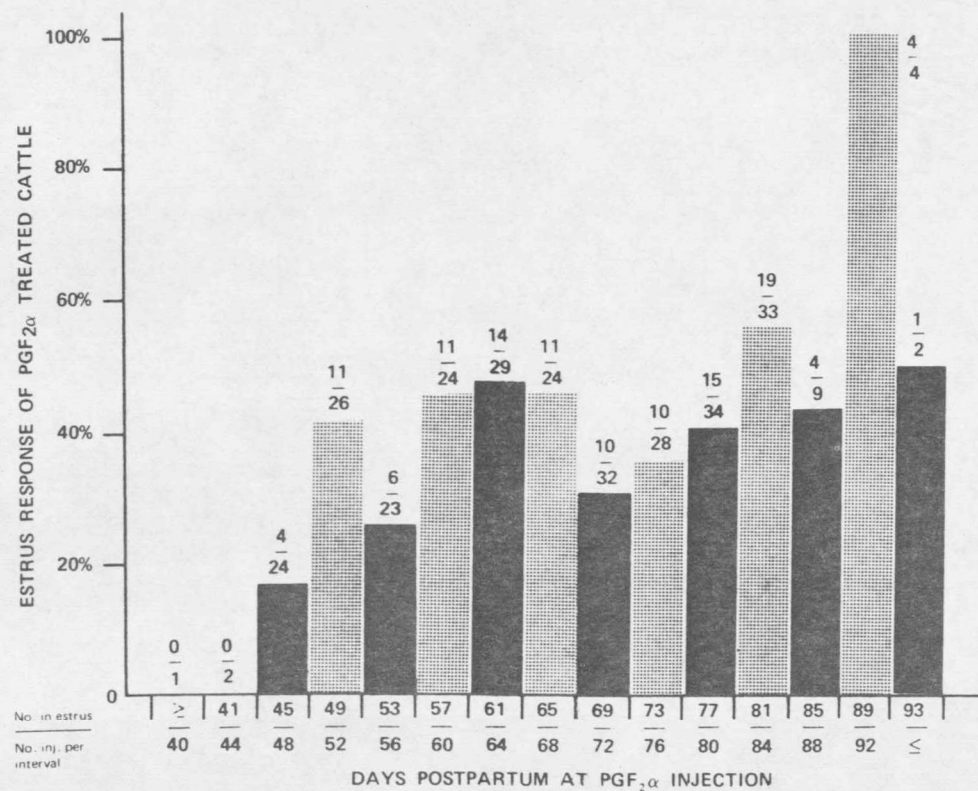


Figure 7. Estrus response of PGF_{2α} treated cattle vs. days for mature cows in the 1974 and 1975 breeding seasons (combined analysis).

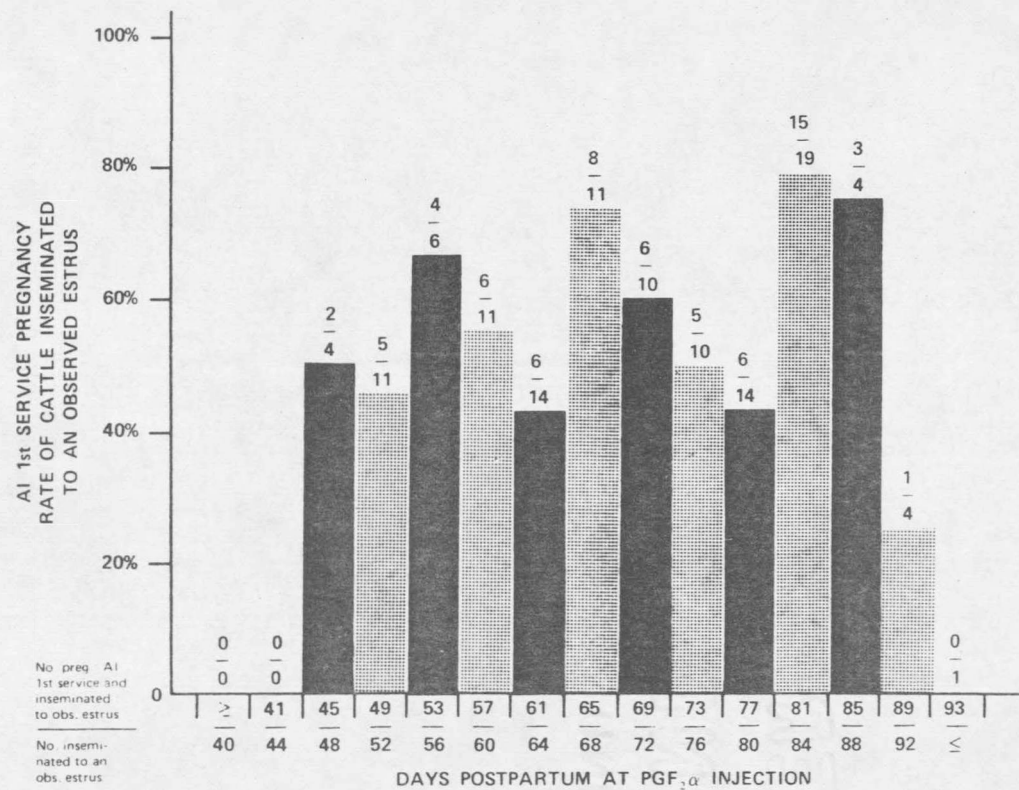


Figure 8. AI 1st service pregnancy rate of cattle inseminated to an observed estrus vs. days postpartum on the day of PGF_{2α} injection for mature cows in the 1974 and 1975 breeding seasons (combined analysis).

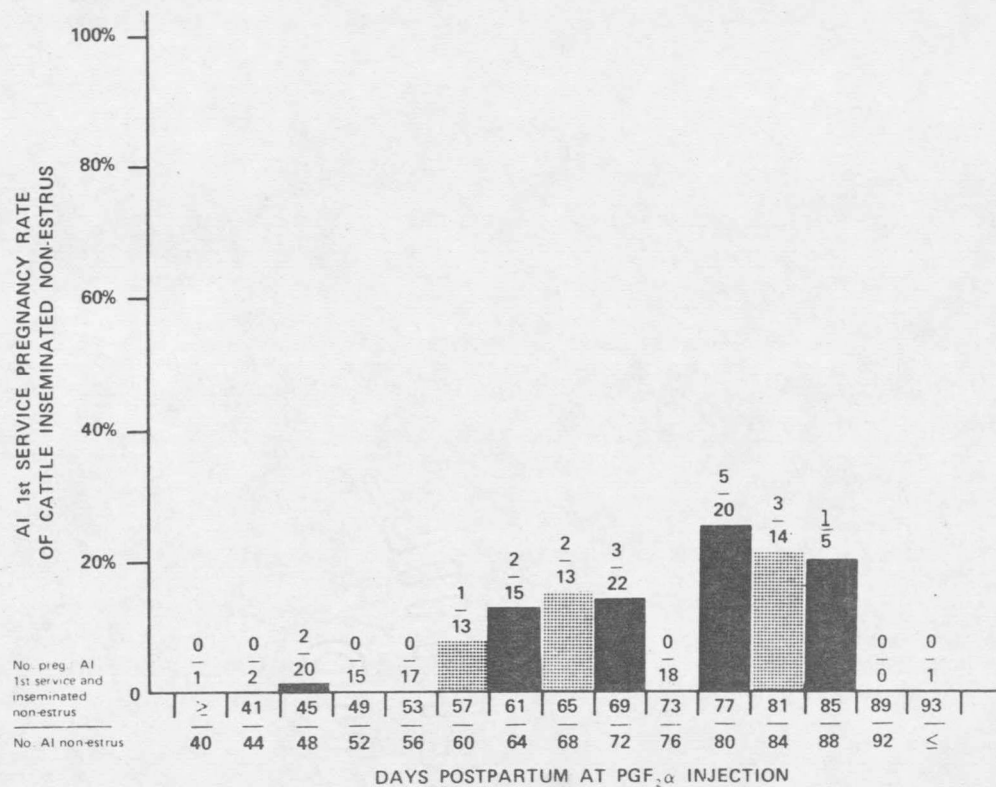
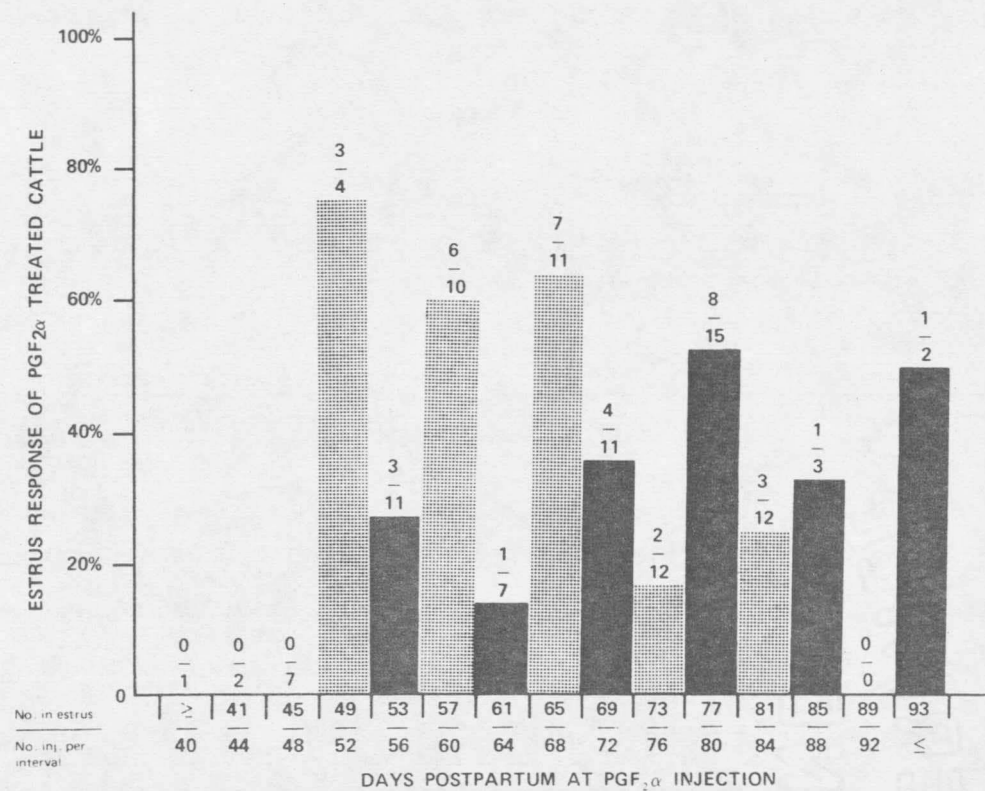
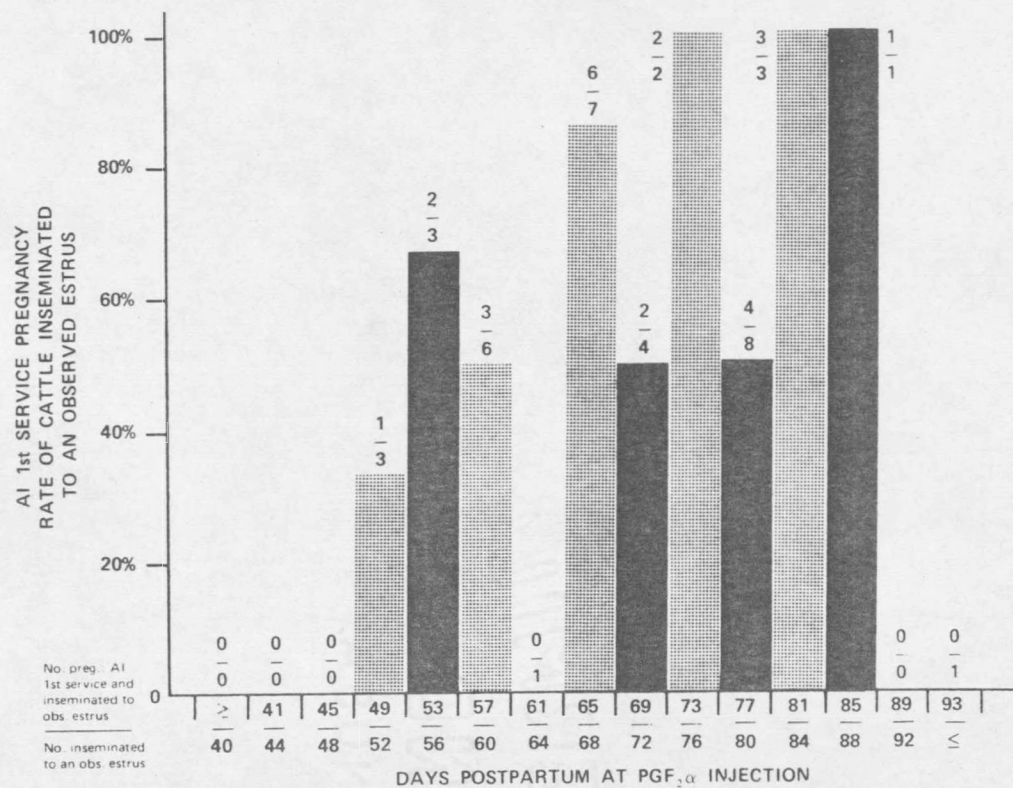


Figure 9. AI 1st service pregnancy rate of cattle inseminated non-estrus vs. days postpartum on the day of PGF₂α injection for mature cows in the 1974 and 1975 breeding seasons (combined analysis).

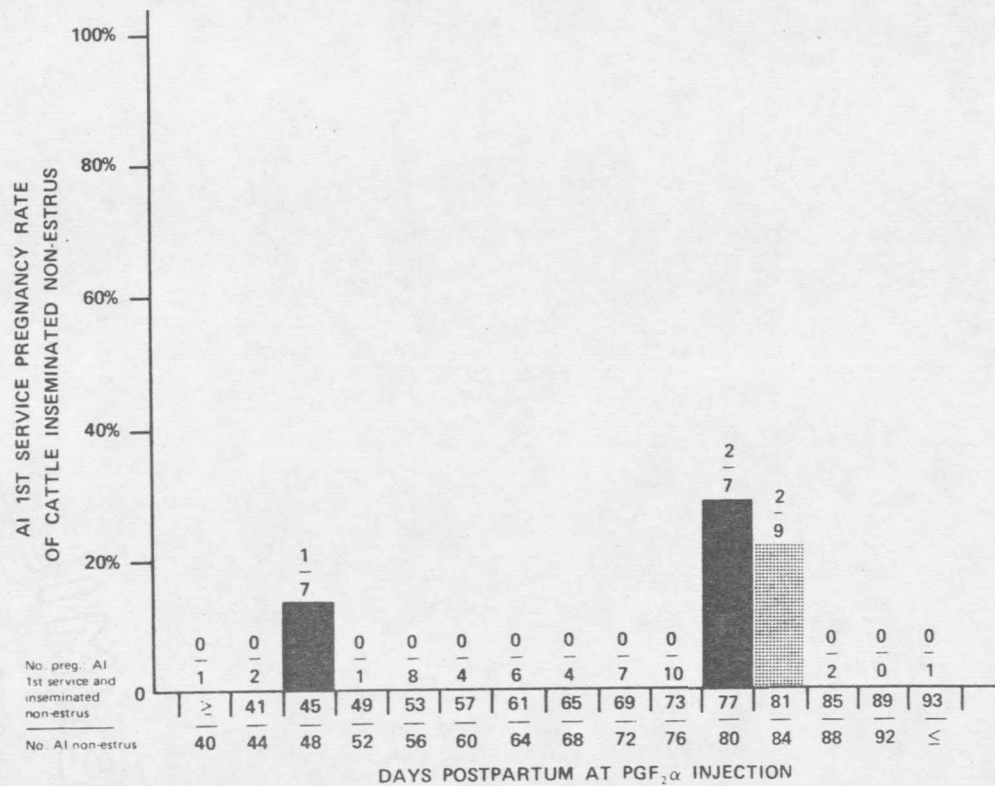
APPENDIX



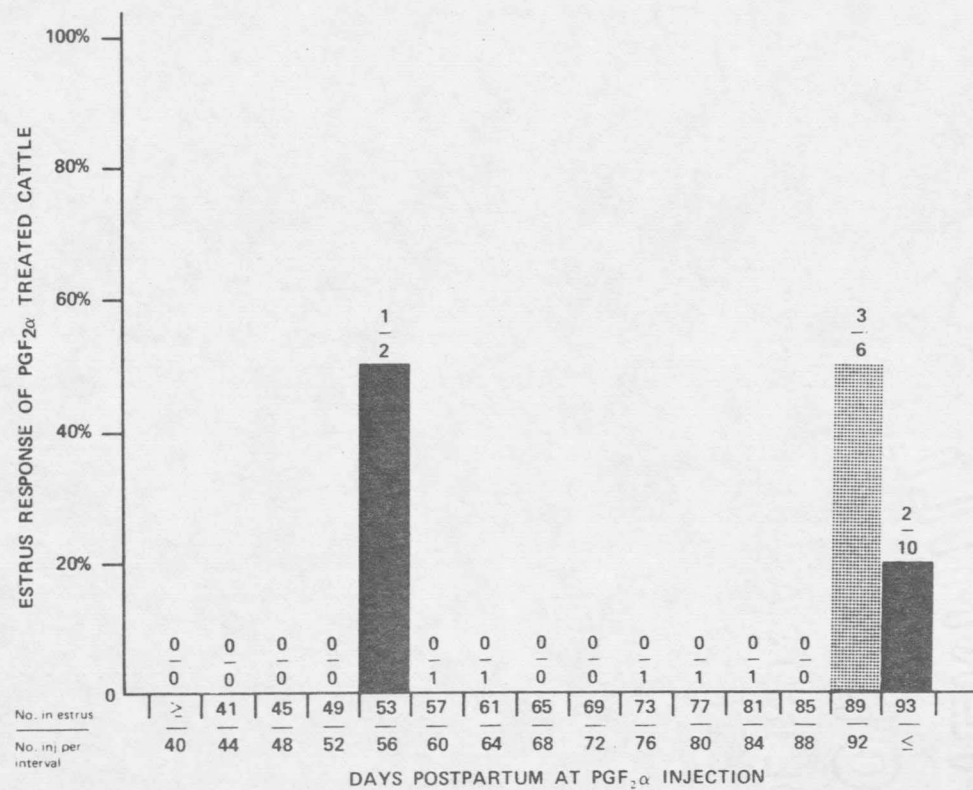
Appendix Figure 1. Estrus response of PGF α treated cattle vs. days postpartum on the day of PGF₂ α injection for mature cows in the spring 1975 breeding season.



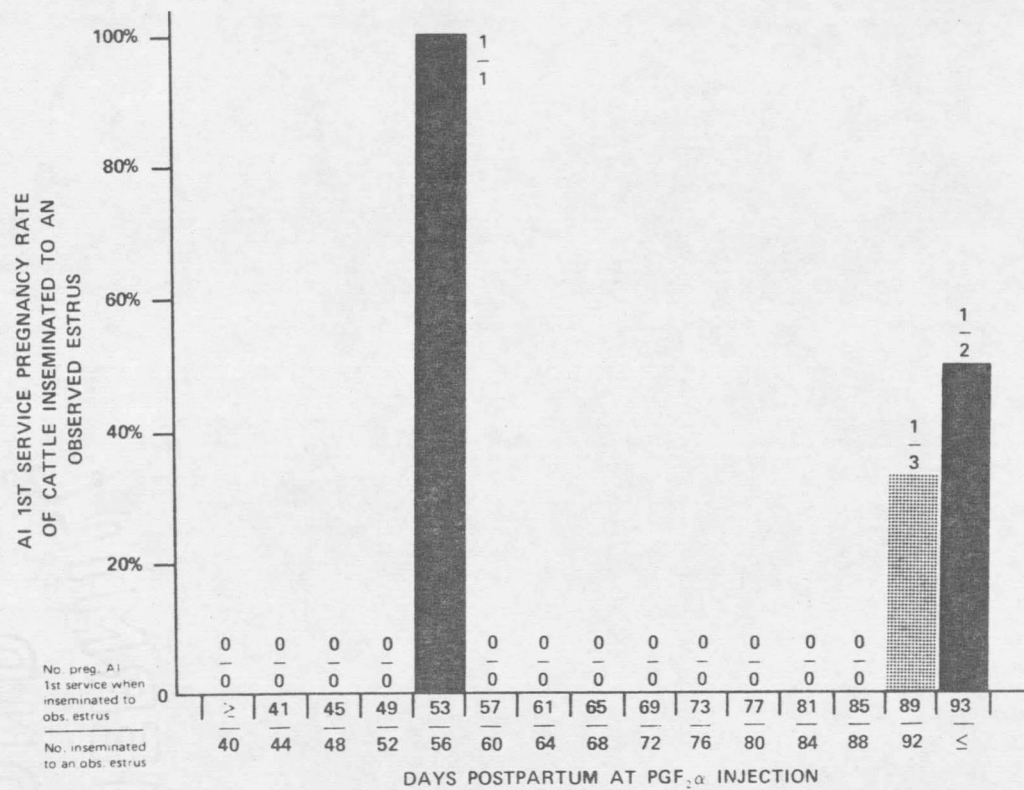
Appendix Figure 2. AI 1st service pregnancy rate of cattle inseminated to an observed estrus vs. days postpartum on the day of PGF₂α injection for mature cows in the spring 1975 breeding season.



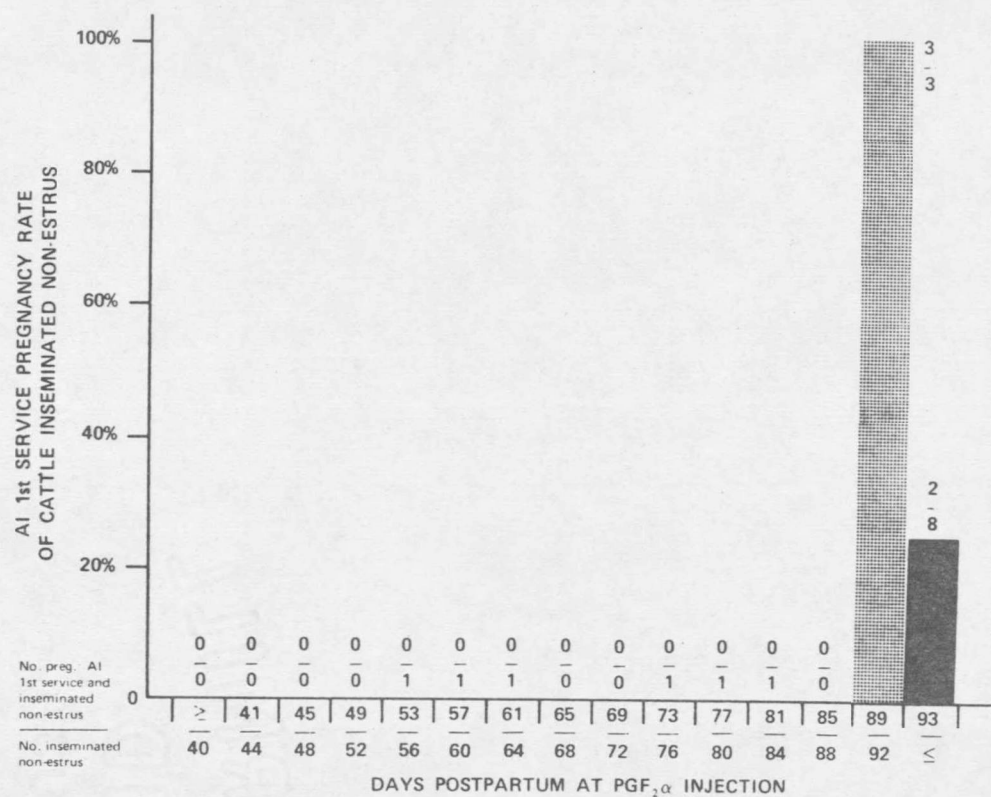
Appendix Figure 3. AI 1st service pregnancy rate of cattle inseminated non-estrus vs. days postpartum on the day of PGF₂α injection for mature cows in the spring 1975 breeding season.



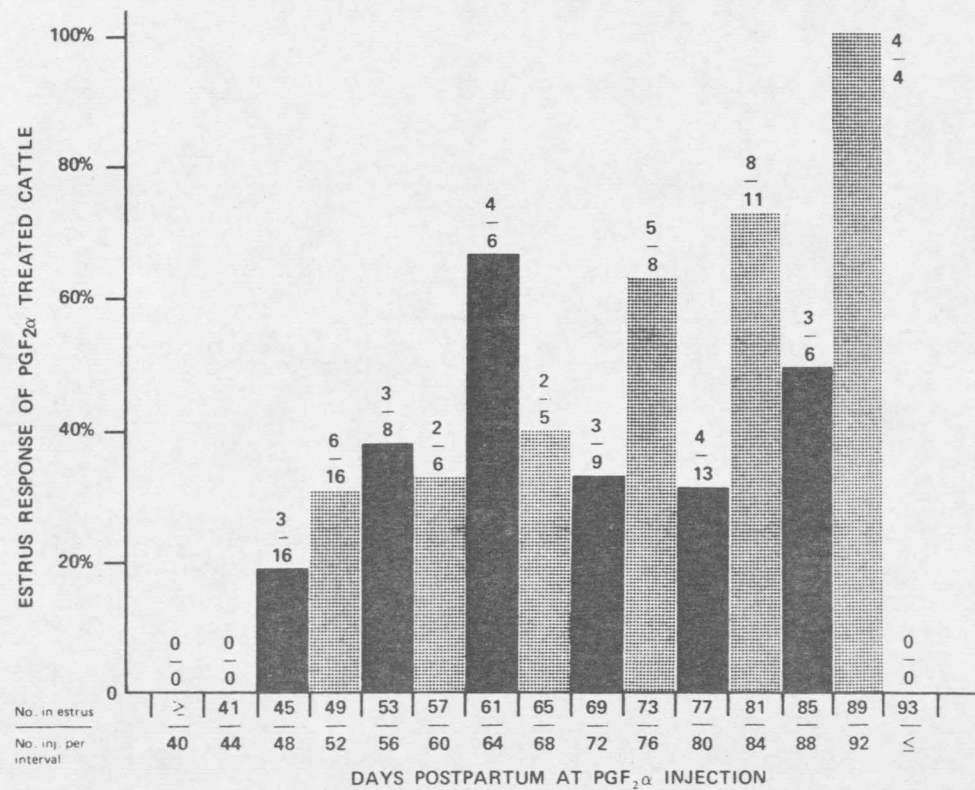
Appendix Figure 4. Estrus response of PGF₂ α treated cattle vs. days postpartum on the day of PGF₂ α injection for 1st calf heifers in the fall 1975 breeding season.



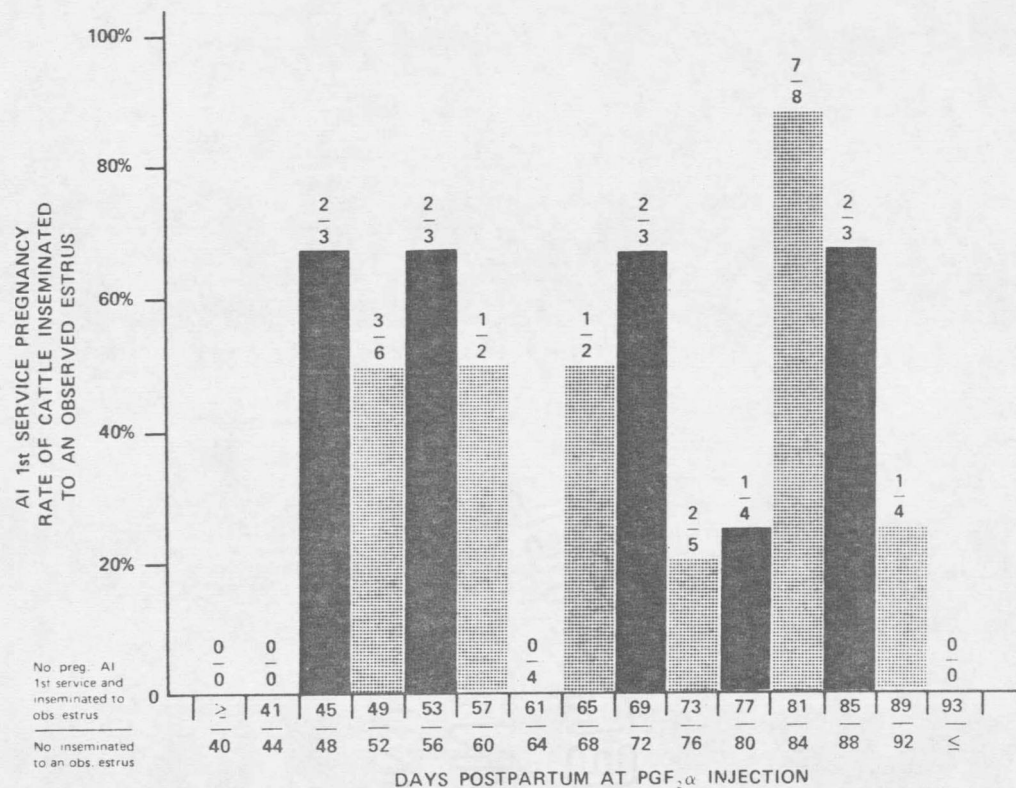
Appendix Figure 5. AI 1st service pregnancy rate of cattle inseminated to an observed estrus vs. days postpartum on the day of PGF₂α injection for 1st calf heifers in the fall 1975 breeding season.



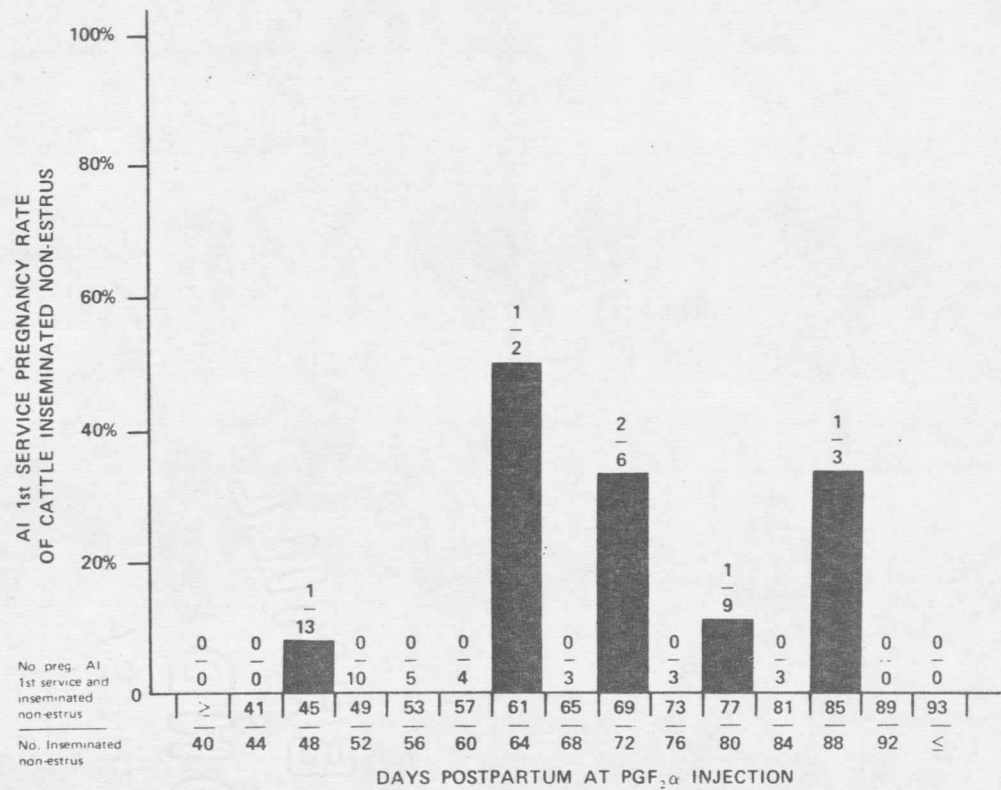
Appendix Figure 6. AI 1st service pregnancy rate of cattle inseminated non-estrus vs. days postpartum on the day of PGF₂α injection for 1st calf heifers in the fall 1975 breeding season.



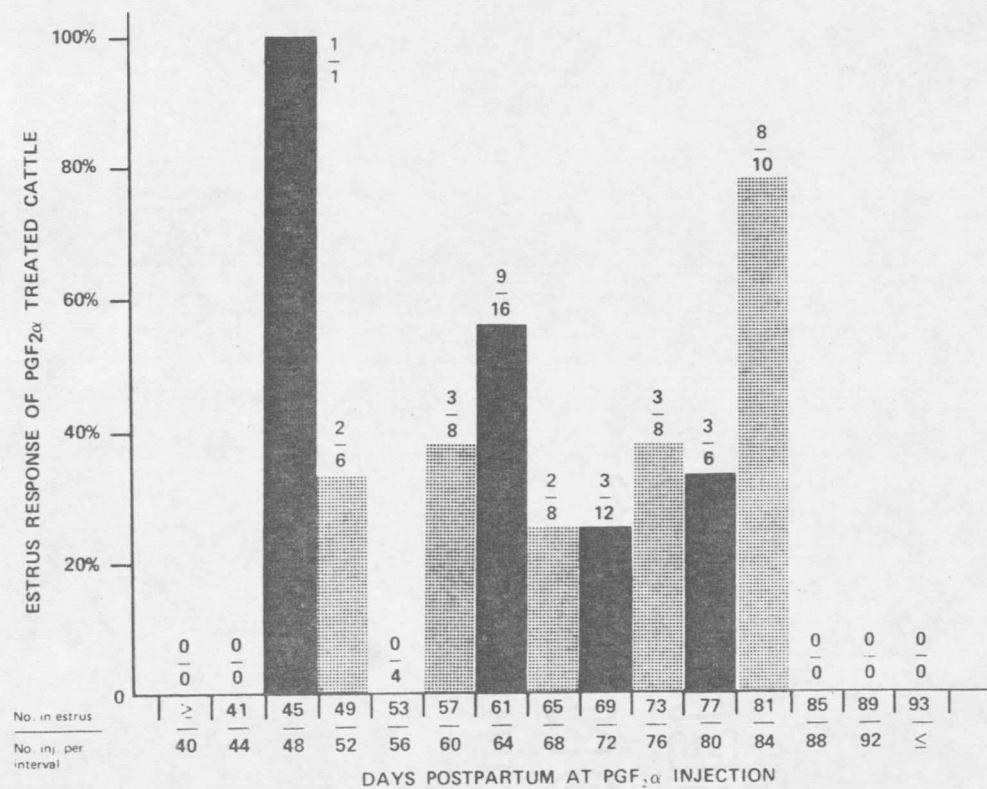
Appendix Figure 7. Estrus response of PGF₂α treated cattle vs. days postpartum on the day of PGF₂α injection for mature cows in the fall 1975 breeding season.



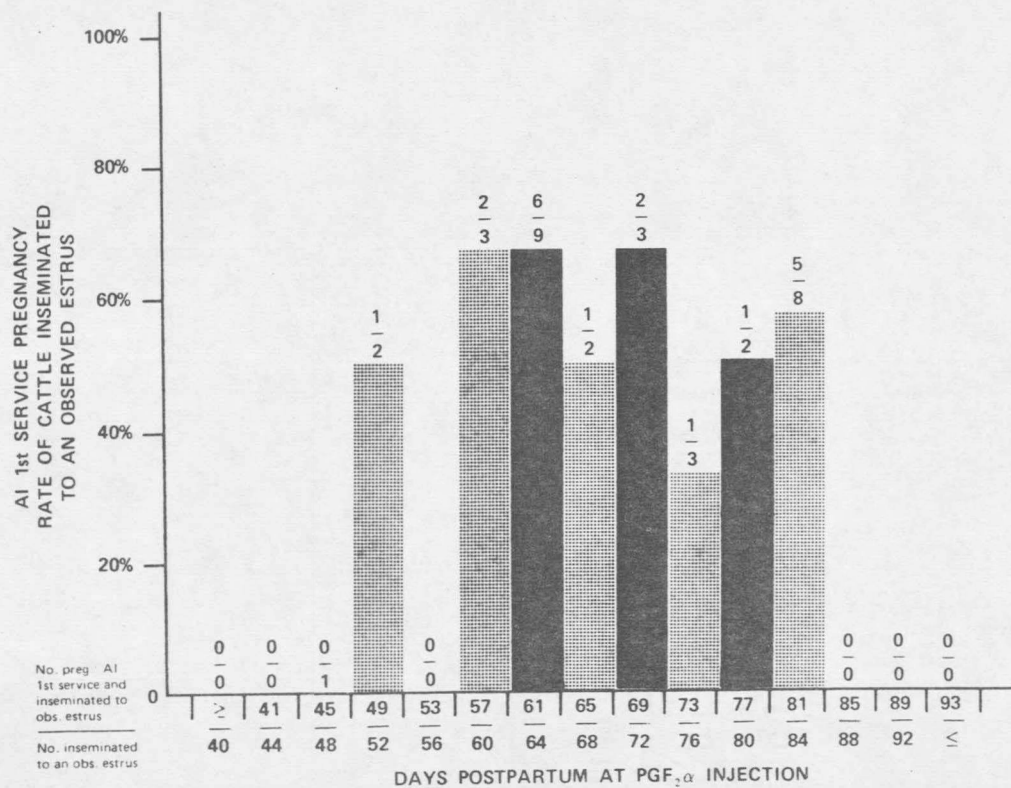
Appendix Figure 8. AI 1st service pregnancy rate of cattle inseminated to an observed estrus vs. days postpartum on the day of PGF₂α injection for mature cows in the fall 1975 breeding season.



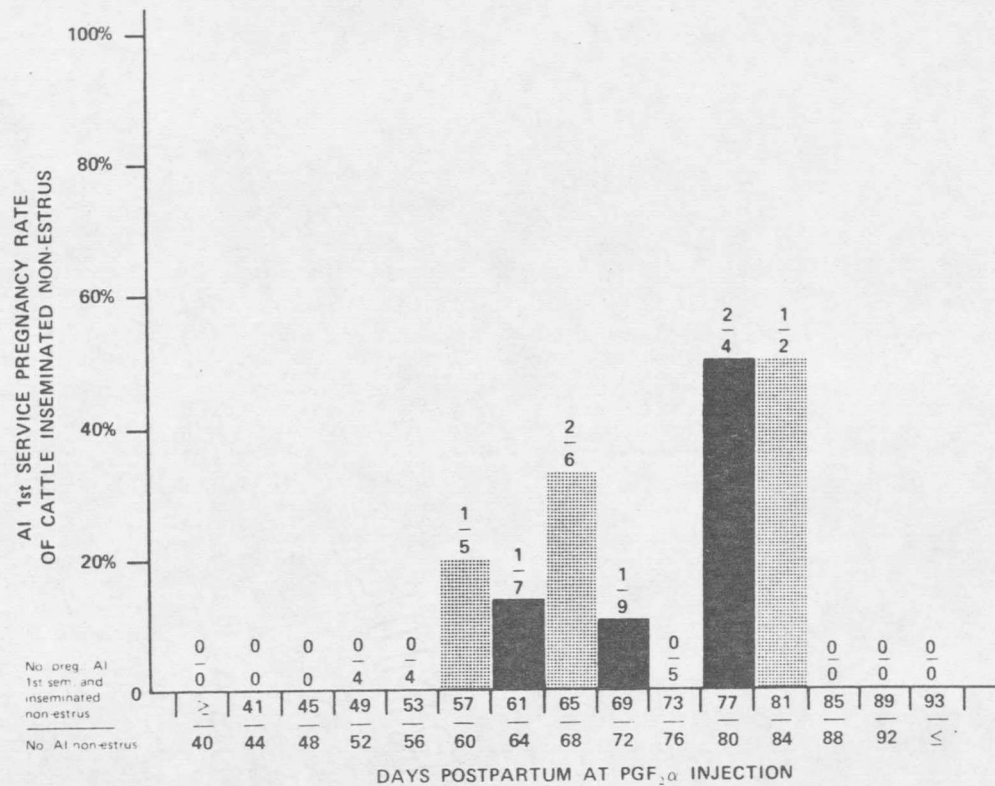
Appendix Figure 9. AI 1st service pregnancy rate of cattle inseminated non-estrus vs. days postpartum on the day of PGF₂α injection for mature cows in the fall 1975 breeding season.



Appendix Figure 10. Estrus response of $\text{PGF}_{2\alpha}$ treated cattle vs. days postpartum on the day of $\text{PGF}_{2\alpha}$ injection for mature cows in the fall 1974 breeding season.



Appendix Figure 11. AI 1st service pregnancy rate of cattle inseminated to an observed estrus vs. days postpartum on the day of PGF₂α injection for mature cows in the fall 1974 breeding season.



Appendix Figure 12. AI 1st service pregnancy rate of cattle inseminated non-estrus vs. days postpartum on the day of PGF₂α injection for mature cows in the fall 1974 breeding season.

LITERATURE CITED

LITERATURE CITED

- Anderson, L. L., R. L. Butcher and R. M. Melampy. 1961. Subtotal hysterectomy and ovarian function in gilts. *Endocrinology*, 69:571.
- Anderson, L. L. 1962. Effect of uterine distention on the estrous cycle of the gilt. *J. Anim. Sci.* 21:597.
- Anderson, L. L., R. L. Butcher and R. M. Melampy. 1963. Uterus and occurrence of oestrus in pigs. *Nature (London)* 198:311.
- Babcock, J. C. 1966. Luteotropic and luteolytic mechanisms in bovine corpora lutea. In "Ovarian Regulatory Mechanisms". *J. Reprod. Fertil. Suppl.* 1:47.
- Barley, D. A., R. L. Butcher and E. K. Inskeep. 1966. Local uterine regulation of luteal regression. *J. Anim. Sci.* 25:918.
- Binder, D., J. Bowler, E. D. Brown, N. S. Crossley, J. Hutton, M. Senior, L. Slater, P. Wilkinson and N. C. A. Wright. 1974. 16-Aryloxyprostaglandins: a new class of potent luteolytic agent. *Prost.* 6:87.
- Blatchley, F. R. and B. T. Donovan. 1969. Luteolytic effect of prostaglandin in guinea-pig. *Nature (London)* 221:1065.
- Blatchley, F. R., B. T. Donovan, N. L. Poyser, E. W. Horton, C. J. Thompson and M. Los. 1971. Identification of prostaglandin $F_{2\alpha}$ in the utero-ovarian blood of guinea-pig after treatment with oestrogen. *Nature (London)*, 230:243.
- Brunner, M. A., L. E. Donaldson and W. Hansel. 1969. Exogenous hormones and luteal function in hysterectomized and intact heifers. *J. Dairy Sci.* 52:1849.
- Burfening, P. J., D. C. Anderson, R. L. Friedrich and J. Williams. 1976. Fertility of cows treated with $PGF_{2\alpha}$ and GnRH. *Proc. West. Sec. Amer. Soc. Anim. Sci.* 27:209.

- Burrell, C., J. N. Wiltbank, D. G. Lefever and G. Rodeffer. 1972. Ear implant (SC21009) for estrous control in heifers. Proc. West. Sec. Amer. Soc. Anim. Sci. 23:547.
- Butcher, R. L., K. Y. Chu and R. M. Melampy. 1962. Utero-ovarian relationships in the guinea-pig. Endocrinology 71:810.
- Caldwell, B. V., R. S. Mazer and P. A. Wright. 1967. Luteolysis as affected by uterine transplantation in the syrian hamster. Endocrinology 80:477.
- Caldwell, B. V., L. E. A. Rowson, R. M. Moor and M. F. Hay. 1969. The utero-ovarian relationship and its possible role in infertility. J. Reprod. Fert., Suppl. 8:59.
- Caldwell, B. V. 1970. The role of the uterus in the regulation of ovarian periodicity. In: Gibian, H. and E. J. Plotz (Ed.) Mammalian Reproduction (1st Ed.). Springer-Verlag, New York, Heidelberg, Berlin.
- Chau, E. 1972. The dragon and the golden Phoenix (Translation: New York, 1972.).
- Christian, R. E. and L. E. Casida. 1948. The effects of progesterone in altering the estrous cycle of the cow. J. Anim. Sci. 7:540.
- Clegg, M. T. 1959. Factors affecting gestation length and parturition. In: H. H. Cole and P. T. Cupps (Ed.) Reproduction in Farm Animals. Vol. I. Academic Press, N.Y.
- Cooper, M. T. 1974. Control of oestrus cycles of heifers with a synthetic prostaglandin analogue. Vet. Rec. 95:200.
- Dhindsa, D. S., A. S. Hoversland and E. P. Smith. 1967. Estrus control and calving performance in beef cattle fed 6-methyl-17-acetoxypregesterone under ranch conditions. J. Anim. Sci. 26:167.
- Diehl, J. R. and B. N. Day. 1973. Effect of prostaglandin $F_{2\alpha}$ on luteal function in swine. J. Anim. Sci., 37:307 (Abstr.).
- Dingle, J. T., M. F. Hay and R. M. Moor. 1968. Lysosomal function in the corpus luteum of the sheep. J. Endocrinol. 40:325.
- Donaldson, L. E. and W. T. Hansel. 1965. Histological study of bovine corpora lutea. J. Dairy Sci. 48:905.

- Douglas, R. H. and J. Ginther. 1972. Effect of prostaglandin $F_{2\alpha}$ on length of diestrus in mares. *Prostaglandins* 2:265.
- Dukes, M., W. Russell and A. L. Walpole. 1974. Potent luteolytic agents related to prostaglandin $F_{2\alpha}$. *Nature (London)*. 250:330.
- Du Mesnil du Buisson, F. 1961. Possibility' d'un fonctionnement dissemblable des ovaires pendant la gestation chez la truie. *C. R. Acad. Sci. (Paris)*. 253:727.
- Du Mesnil du Buisson, F. 1966. Discussion. Colloque international sur la physiologie de la reproduction chez les mammiferes. Paris.
- Eliasson, R. 1959. Studies on prostaglandins. Occurrence, formation and biological actions. *Acta Physiol. Scand.*, 46: Suppl. 158:1.
- Ellicott, A. R., J. R. Hill, Jr. and C. E. Thompson. 1975. Appointment of the hour of mating in the cow. *J. Anim. Sci.* 41:351 (Abstr.).
- Fahning, M. L., R. H. Shultz, E. F. Granham, J. D. Donker and H. W. Mohrenweiser. 1966. Synchronization of oestrus in dairy heifers with 6-methyl-17-acetoxypregesterone and its effect on conception rate. *J. Reprod. Fert.* 12:569.
- Ginther, O. J. 1967. Local utero-ovarian relationships. *J. Anim. Sci.* 26:578.
- Ginther, O. J. and G. E. Bisgard. 1972. Role of the main uterine vein in local action of an interuterine device on the corpus luteum in sheep. *Amer. J. Vet. Res.*, 33:1583.
- Goding, J. R., M. D. Cain, J. Cernini, M. Cerini, W. A. Chamley and I. A. Cumming. 1972. Prostaglandin $F_{2\alpha}$ "The" luteolytic hormone in the ewe. *J. Reprod. Fert.* 28:146. (Abstr.).
- Goldblatt, M. W. 1933. A depressor substance in seminal fluid. *Chem. Ind.* 52:1056.
- Gomes, W. R. and R. E. Erb. 1965. Progesterone in bovine reproduction. A Review. *J. Dairy Sci.* 48:314.

- Graves, N. W., T. G. Dunn, C. C. Kaltenbach, R. E. Short and J. B. Carr. 1975. Estrus and ovulation with prostaglandin $F_{2\alpha}$, norgestamet, and gonadotrophin releasing hormone. Proc. West. Sec. Amer. Soc. Anim. Sci. 26:193.
- Greenstein, J. S., R. W. Murray and R. C. Foley. 1958. Effect of exogenous hormones on the reproductive processes of the cycling dairy heifer. J. Dairy Sci. 41:1834. (Abstr.).
- Gutknecht, G. A., L. J. Whygarden and B. B. Pharriss. 1971. The effect of $PGF_{2\alpha}$ on ovarian and plasma progesterone level in the pregnant hamster. Proc. Soc. Exp. Biol. Med. 136:1151.
- Hafs, H. E., T. M. Louis, P. A. Noden and W. D. Oxender. 1974. Control of the estrous cycle with prostaglandin $F_{2\alpha}$ in cattle and horses. J. Anim. Sci. 38:10 (Suppl. 1).
- Hafs, H. D., J. G. Mans and G. E. Lemming. 1975. Fertility of cattle from AI after $PGF_{2\alpha}$. J. Anim. Sci. 41:355 (Abstr.).
- Hansel, W. and W. C. Wagner. 1960. Luteal inhibition in the bovine as a result of oxytocin injections, uterine dilation and intra-uterine infusions of seminal and preputial fluids. J. Dairy Sci. 43:796.
- Hansel, W. and P. V. Malven. 1960. Estrus cycle regulation in beef cattle by orally active progestational agents. J. Anim. Sci. 19:1324 (Abstr.).
- Hansel, W., P. V. Malven and D. L. Black. 1961. Estrus cycle regulation in the bovine. J. Anim. Sci. 20:621.
- Hansel, W., P. W. Concannon and J. H. Lukaszewska. 1973. Corpora lutea of large domestic animals. Biol. Reprod. 8:222.
- Harley, G. W. 1941. Native African Medicine with Special Reference to its Practice in the Mano Tribe of Liberia. (Cambridge, Mass: Harvard University Press). 237-238.
- Harms, P. G. and P. V. Malven. 1969. Modification of bovine luteal function by exogenous oxytocin and progesterone. J. Anim. Sci. 29:25.
- Harris, G. W. and H. J. Campbell. 1966. The regulation of the secretion of luteinizing hormone and ovulation. In: The Pituitary Gland. Harris and Donovan. Univ. Calif. Press, Berkeley, Calif. 2:99.

- Hawk, H. W. and D. J. Bolt. 1970. Luteolytic effect of estradiol 17-B when administered after midcycle in the ewe. Biol. Reprod. 2:275.
- Hearnshaw, H., P. E. Mattner, C. D. Nancarrow and B. J. Restall. 1974. The effect of the mode of administration of prostaglandin $F_2\alpha$ on the synchronization of oestrus in cattle. J. Reprod. Fert. 36:486.
- Hechter, O., M. Fraenkel, M. Lev and S. Soskin. 1940. Influence of the uterus on the corpus luteum. Endocrinology 26:680.
- Hersche, G., Jr., G. H. Kiracafe, R. M. McKee, D. C. Davis and G. R. Brower. 1974. Control of estrus in heifers with $PGF_2\alpha$ and syncromate B. J. Anim. Sci. 38:225.
- Henderson, K. M., and K. P. McNatty. 1975. A biochemical hypothesis to explain the mechanism of luteal regression. Prost. 9:779.
- Henricks, D. M., J. T. Long, J. R. Hill and J. F. Dickey. 1974. The effect of prostaglandin $F_2\alpha$ during various stages of the oestrus cycle of beef heifers. J. Reprod. Fert. 41:113.
- Hichens, M., D. L. Grinwich and R. R. Behrman. 1974. $PGF_2\alpha$ induced loss of corpus luteum gonadotrophin receptors. Prost. 7:457.
- Inskip, E. K. 1973. Potential uses of prostaglandins in control of reproductive cycles of domestic animals. J. Anim. Sci. 36:1149.
- Inskip, E. K., J. A. Welch, M. R. McClung, E. A. Linger and J. O. Heishman. 1975. Control of estrus by $PGF_2\alpha$ and estradiol benzoate. J. Anim. Sci. 40:187 (Abstr.).
- Japelli, G. and G. M. Scafa. 1906. Sur les effets des injections intraveineuses d'extrait prostatique de chien. Arch. Ital. Bio. 45:165.
- Kaltenbach, C. C., T. G. Dunn, T. E. Kiser, L. R. Corah, A. M. Akbar and G. D. Niswender. 1974. Release of FSH and LH in beef heifers by synthetic gonadotrophin releasing hormone. J. Anim. Sci. 38:357.
- Karim, S. M. M. 1975. Prostaglandins and Reproduction. (1st Ed.). University Park Press Chamber of Commerce Building, Baltimore, Maryland, 21202.

- Kenney, R. M. 1964. Histochemical and biochemical correlates of the estrous cycle in the normal cyclic uterus and ovary of the cow. Cornell University Thesis (307 pages).
- King, G. J. and H. A. Robertson. 1974. A two injection schedule with prostaglandin $F_{2\alpha}$ for the regulation of the ovulatory cycle of cattle. *Theriogenology*, 1:123.
- Kinkie, R. A., D. C. Anderson, E. L. Moody and P. J. Burfening. 1976. Breeding heifers by appointment with $PGF_{2\alpha}$ and GnRH. *Proc. West. Sec. Amer. Soc. Anim. Sci.* 27:205.
- Kirton, K. T., B. B. Pharriss and A. D. Forbes. 1970. Luteolytic Effects on prostaglandin $F_{2\alpha}$ in primates (34464). *Proc. Soc. Exp. Biol. Med.* 133:314.
- Labhsetwar, A. P. 1971. Luteolysis and ovulation induced by prostaglandin $F_{2\alpha}$ in the hamster. *Nature (London)* 230:528.
- Lambert, P. W., D. P. Griswold, V. A. LaVoie and E. L. Moody. 1975. AI beef management of $PGF_{2\alpha}$ controlled estrus. *Proc. West. Sec. Amer. Soc. Anim. Sci.* 26:181.
- Lambert, P. W., W. M. Greene, J. D. Strickland, D. K. Han and E. L. Moody. 1976. $PGF_{2\alpha}$ controlled estrus in beef cattle. *Proc. West Sec. Amer. Soc. Anim. Sci.* 27:211.
- Lamond, D. R., R. V. Tomlinson, M. Drost, D. M. Henricks and W. Jochle. 1973. Studies of $PGF_{2\alpha}$ in the cow. *Prostaglandins* 4:269.
- Lauderdale, J. W. 1972. Effects of $PGF_{2\alpha}$ on pregnancy and estrous cycle of cattle. *J. Anim. Sci.* 35:246 (Abstr.).
- Lauderdale, J. W. 1974. Distribution and biological effects of prostaglandins. *J. Anim. Sci.* 38:22 (Suppl. I).
- Lauderdale, J. W., B. E. Sequin, J. N. Stellflug, J. R. Chenault, W. W. Thatcher, C. K. Vincent and A. F. Loyancano. 1974. Fertility of cattle following $PGF_{2\alpha}$ injection. *J. Anim. Sci.* 38:964.

- LaVoie, V. A., G. R. Poncelet, D. K. Han, C. L. Soliday, P. W. Lambert and E. L. Moody. 1975. Effect of PGF₂ α on the estrous cycle, corpora lutea and progesterone levels of hysterectomized cows. J. Anim. Sci. 41:166.
- Liehr, R. A., E. B. Marion and H. H. Olson. 1972. Effects of prostaglandin on cattle estrous cycles. J. Anim. Sci. 35:247.
- Loeb, L. 1923. The effect of extirpation of the uterus on the life and function of the corpus luteum in the guinea-pig. Proc. Soc. Exp. Biol. Med. 20:441.
- Louis, T. M., H. D. Hafs and B. E. Sequin. 1973. Progesterone LH, estrus and ovulation after prostaglandin F₂ α in heifers. Proc. Soc. Exp. Biol. Med. 143:152.
- Lynn, J. E., W. E. Collins, E. K. Inskeep, W. H. McShan, and L. E. Casida. 1965. Effects of Gonadotropins, oxytocin and glucose on the bovine corpus luteum at the fourteenth day of the estrual cycle. J. Anim. Sci. 24:790.
- Malven, P. V. and W. Hansel. 1964. Ovarian function in dairy heifers following hysterectomy. J. Dairy Sci. 47:1388.
- Manns, J. G., M. S. Wenkoff and W. M. Adams. 1976. Time of AI on fertility of heifers treated with PGF₂ α . J. Anim. Sci. 43:295 (Abstr.).
- Mazer, R. S., and P. A. Wright. 1968. A hamster uterine luteolytic extract. Endocrinology 83:1065.
- McCracken, J. A., M. E. Glew and R. J. Scaramuzzi. 1970. Corpus luteum regression induced by prostaglandin F₂ α . J. Clin. Endocr. Metab. 30:544.
- McCracken, J. A., D. T. Baird and J. R. Goding. 1971. Factors affecting the secretion of steroids from the transplanted ovary in the sheep. Rec. Prog. Horm. Res., 27:537.
- McCracken, J. A., J. C. Carlson, M. E. Glew, J. R. Goding, D. T. Baird, K. Green and B. Samuelsson. 1972. Prostaglandins F₂ α identified as a luteolytic in sheep, Nature New Biol., 238:129.
- Melampy, R. M. and L. L. Anderson. 1968. Role of the uterus in corpus luteum function. J. Anim. Sci. 27:77 (Suppl. I).

- Moor, R. M. 1968. Effect of embryo on corpus luteum function. J. Anim. Sci. Suppl. 1:97.
- Nellor, J. E., J. E. Ahrenhold and R. H. Nelson. 1960. Influence of oral administration of 6-methyl-17-acetoxypregesterone on follicular growth and estrous behavior in beef heifers. J. Anim. Sci. 19:1331 (Abstr.).
- Nelms, G. E. and W. Combs. 1961. Estrus and fertility in beef cattle subsequent to the oral administration of 6-methyl-17-acetoxypregesterone. J. Anim. Sci. 20:975 (Abstr.).
- Niswender, G. D., T. M. Nett and A. M. Akbar. 1974. The hormones of reproduction. In: E. S. E. Hafez (Ed.) Reproduction in Farm Animals. (3rd Ed.). Lea and Febiger, Philadelphia.
- O'Grady, J. P., E. I. Kohorn, R. H. Glass, B. V. Caldwell, W. A. Brock and L. Speroff. 1972. Inhibition of progesterone synthesis in vitro by prostaglandin $F_{2\alpha}$. J. Reprod. Fert. 30:153.
- Pharriss, B. B., and J. L. Wyngarden. 1969. The effect of $PGF_{2\alpha}$ on the progestogen content of ovaries from pseudopregnant rats. Proc. Soc. Exp. Biol. Med., 130:92.
- Pharriss, B. B. 1970. The possible vascular regulation of luteal function. Perspect. Biol. Med. 13:434.
- Pharriss, B. B., J. Cornette and G. D. Gutknecht. 1970. Vascular control of luteal steroidogenesis. J. Reprod. Fert., Suppl. 10:97.
- Pharriss, B. B., S. H. Tillson and R. R. Erickson. 1972. PG's in luteal function. Rec. Prog. Horn. Res., 28:51-89.
- Poyser, N. ., E. W. Horton, C. J. Thompson and M. Los. 1971. Identification of $PGF_{2\alpha}$ released by distension of guinea-pig uterus in vitro. Nature (London), 230:526.
- Reeves, J., J. E. Kinder, G. K. Tarnaysky, P. K. Chakraborty, D. Coy and A. V. Schally. 1975. Synchronized breeding in cows with $PGF_{2\alpha}$ and LH-RH/FSHRH analog. J. Anim. Sci. 41:376 (Abstr.).
- Roche, J. F. 1974. Synchronization of oestrus and fertility following artificial insemination in heifers given prostaglandin $F_{2\alpha}$. J. Reprod. Fert. 37:135.

- Rowson, L. E. A. and R. Moor. 1964. Effect of partial hysterectomy on the length of the diestrous interval in sheep. Proc. V. Congr. Internaz. Riprod. Anim. Fecond. Artif. 2:393.
- Rowson, L. E. A., and R. M. Moor. 1967. The influence of embryonic tissue homogenate infused into the uterus on the lifespan of the corpus luteum in the sheep. J. Reprod. Fert. 13:511.
- Rowson, L. E. A., R. Tervit and A. Brand. 1972. The use of prostaglandins for synchronization of estrous in cattle. J. Reprod. Fert. 29:145 (Abstr.).
- Schmidt, W., D. Schams, B. Hoffmann, R. Hamburger, H. Karg. 1975. (Sudd, Versuchs-und forschungsanstalt fur Milchwirtschaft, Institut fur Physiologie, Techn. Universitat Munchen, D 805 Freising-Weiherstephan) und O. Gunzler (Tiergesundheitsdienst Bayern D 8011 Grub, Post Poing).
- Schneider, W. P. 1975. The chemistry of the prostaglandins In: Progress in Research. Vol. II (S.M.M. Karim, editor) (Lancaster; M.T.P.).
- Schwartz, N. B. 1974. The role of FSH and LH and of their antibodies on follicle growth and on ovulation. Biol. of Reprod. 10:236.
- Short, R. V. 1972. Role of Hormones in sex cycles. In: C. R. Austin and R. V. Short (Ed.) Reproduction in Mammals # 3 Hormones in Reproduction. Cambridge University Press.
- Stellflug, J. N., T. M. Louis, B. E. Sequin and H. D. Hafs. 1973. Luteolysis after 30 or 60 mg PGF₂ α in heifers. J. Anim. Sci. 37:330 (Abstr.).
- Stellflug, J. N., T. M. Louis, H. D. Hafs and B. E. Sequin. 1975. Luteolysis, estrus and ovulation and blood prostaglandin F after intramuscular administration of 15, 30 or 60 mg prostaglandin F₂ α . Prost. 9:609.
- Strott, C. A., T. Yoshimi, G. T. Ross, M. B. Lipsett. 1969. Ovarian Physiology: Relationship between plasma LH and Stereognosis by the Follicle and Corpus Luteum. Effect of HCG. J. Clin. Endocr. and Meta. 29:1157.

- Territ, H. R., L. E. A. Rowson and A. Brand. 1973. Synchronization of oestrus in cattle using a prostaglandin $F_{2\alpha}$ analogue (ICI 79939). J. Reprod. Fert., 34:179.
- Trimberger, G. W. and W. Hansel. 1955. Conception rate and ovarian function following estrus control by progesterone injections in dairy cattle. J. Anim. Sci. 14:224.
- Ulberg, L. C. and C. E. Lindley. 1960. Use of progesterone and estrogen in the control of reproductive activities in beef cattle. J. Anim. Sci. 19:1132.
- Van Niekerk, C. H., P. C. Belonze and J. C. Morgenthal. 1974. Oestrus synchronization in cattle using progesterone and a PGF analogue. Theriogenology 2:73.
- Von Euler, U. S. 1934. Zur kenntnis der pharmakologischen Wirkung von nalive sekret en und extrakten mannlicher accessorischer Geschlechtsdrusen. Arch. Exp. Path. Pharmac., 175:78.
- Von Euler, U. S. 1936. On the specific vasodilating and plain muscle stimulating substance from accessory glands in man and certain animals (Prostaglandin and vesiglandin). J. Physiol. (London) 88:213.
- Wagner, W. C., R. E. Strobbehn and P. A. Harris. 1971. ACTH and corticoid treatment on bovine CL function. J. Anim. Sci. 33:1163 (Abstr.).
- Weinsbenker, N. M. and N. H. Anderson. 1973. Chemistry. In: The Prostaglandin, Vol. 1, 5-82 (P. W. Ramwell, Ed.) (London: Plenum Press).
- Welch, J. A., A. J. Hackett, C. J. Cunningham, J. O. Heishman, S. P. Ford, Nadaraga, W. Hansel and E. K. Inskeep. 1975. Control of estrus in lactating beef cows with PGF $_{2\alpha}$ and estradiol benzoate. J. Anim. Sci. 41:1686.
- Whitman, R. W., J. N. Wiltbank, D. G. Lefever and A. H. Denham. 1972. Ear implant (SC21009) for estrus control in cows. Proc. West. Sec. Amer. Soc. Anim. Sci. 23:280.
- Wilks, J. and W. Hansel. 1971. Oxytocin and the secretion of luteinizing hormone in cattle. J. Anim. Sci. 33:1048.

- Willetts, E. L. 1950. The fertility of heifers following administration of progesterone to alter the estrual cycle. J. Dairy Sci. 33:381 (Abstr.).
- Williams, W. F., J. O. Johnston, M. Lauterbach, and B. Fagan. 1967. Lutolytic effect of a bovine uterine powder on the corpora lutea, follicular development, and progesterone synthesis of the pseudo-pregnant rabbit ovary. J. Dairy Sci. 50:555.
- Wilson, L. Jr., R. J. Cendella, R. L. Butcher and E. K. Inskeep. 1972. Levels of prostaglandins in the uterine endometrium during the ovine estrous cycle. J. Anim. Sci. 34:93.
- Wiltbank, J. N. and L. E. Casida. 1956. Alteration of ovarian activity of hysterectomy. J. Anim. Sci. 15:134.
- Wiltbank, J. N., J. E. Engalls and W. W. Rowden. 1961. Effects of various forms and levels of estrogens alone or in combinations with gonadotrophins on the estrous cycle of beef heifers. J. Anim. Sci. 20:341.
- Wiltbank, J. N., D. R. Zimmerman, J. E. Ingalls and W. W. Rowden. 1965. Use of progestational compounds alone or in combination with estrogen for synchronization of estrus. J. Anim. Sci. 24:990.
- Wishart, D. F. 1974. Synchronization of oestrus in cattle using a potent progestin (SC21009) and PGF₂ α . Theriogenology 1:87.
- Wishart, D. F. and I. M. Young. 1974. Artificial insemination of progestin (SC21009) treated cattle at predetermined times. Vet. Rec. 95:503.
- Woody, C. O., N. L. First and A. L. Pope. 1967. Effect of exogenous progesterone on estrous cycle length. J. Anim. Sci. 26:139.
- Woody, C. O. and O. J. Ginther. 1968. Effect of exogenous progesterone on corpora lutea in unilaterally hysterectomized heifers. J. Anim. Sci. 27:1387.

MONTANA STATE UNIVERSITY LIBRARIES



3 1762 10014689 1



NB75
L174
Cap 2