Fertility of beef cattle after PGF2a controlled estrus in two breeding management systems
by William Mearle Greene

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

Abstract:
Three studies were conducted to evaluate fertility of cattle after Prostaglandin F2*alpha;(PGF2α) controlled estrus. In the first study lactat-ing cows were randomly assigned to either a Conventional system (non-treated controls n=202) or a PGF2α system (n=204). The breeding season for both systems consisted of 25 days artifical insemination (AI) followed by 20 days natural service. Estrus detection was periodic during daylight hours (hrs) and cattle in both systems were bred approximately 12 hours after observed estrus except for the non-estrus breeding of some PGF2α treated cattle. PGF2α (25 mg Prostin F2α) was administered intramuscular (IM) on the 5th day of actual breeding to only those animals in the PGF2α system not detected in estrus prior to injection. Breeding was conducted under the general breeding scheme after PGF2α for 80 hrs at which time all PGF2α animals not previously detected in estrus were bred non-estrus. Pregnancy was determined by rectal palpation. There were no significant differences between breeding systems for total pregnancy (TP), total AI pregnancy (AIP) or AI first service pregnancy rates. The average day of conception for the PGF2α system (day 20) was significantly closer (P<.01) to the start of the breeding season than the conventional system (day 23). In the second study, two trials were conducted using heifers in trial I and lactating cows in trial 2. Animals in both trials were assigned to one of three treatments. Treatment one was non-treated controls and were bred for 45 days natural service. Treatment two received two injections of 15 mg PGF2α (IM) and treatment three received two injections of 25 mg PGF2α (IM) Il days apart. Cattle in treatments 2 and 3 were bred about 74 hours post the second PGF2α injection without regard to estrus. Approximately 48 hours after insemination PGF2α treated cattle were exposed to natural breeding for 18 days. On day 21 of the breeding season bulls were removed and estrus detection commenced. Al resumed on day 22 and continued until day 26 of the breeding season at which time natural service resumed until day 45 of the breeding season. TP rates were determined by rectal palpation. There were no significant differences between treatments 1,2 and 3 for TP. Study three analyzed breeding trials conducted during fall 1974(F74), summer 1975(875), fall 1975(F75) and summer 1976(876) to test the effect of on fertility when administered for 2 years to the same cattle. Methods and materials for this study are similar to study one in all respects except for the F74 nonestrus breeding which occurred at 72 hrs post PGF2α treatment. TP and AIP rates were not different between breeding systems after year 1; however TP and AIP rates were greater (P=.035 and P=.006, respectively) in the PGFg^ system after year 2. In the conventional system TP and AIP rates -decreased (P<.001) from year I to year 2. Similar trends were observed in the PGF2α system for TP(P=.001) and AIP(P>.10) from year 1 to year 2.

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Date May 17, 1977

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A thesis submitted in partial fulfillment
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ABSTRACT

Three studies were conducted to evaluate fertility of cattle after Prostaglandin $F_{2\alpha}$($PGF_{2\alpha}$) controlled estrus. In the first study lactating cows were randomly assigned to either a Conventional system (non-treated controls n=202) or a $PGF_{2\alpha}$ system (n=204). The breeding season for both systems consisted of 25 days artifical insemination (AI) followed by 20 days natural service. Estrus detection was periodic during daylight hours (hrs) and cattle in both systems were bred approximately 12 hours after observed estrus except for the non-estrus breeding of some $PGF_{2\alpha}$ treated cattle. $PGF_{2\alpha}$ (25 mg Prostin $F_{2\alpha}$) was administered intramuscular (IM) on the 5th day of actual breeding to only those animals in the $PGF_{2\alpha}$ system not detected in estrus prior to injection. Breeding was conducted under the general breeding scheme after $PGF_{2\alpha}$ for 80 hrs at which time all $PGF_{2\alpha}$ animals not previously detected in estrus were bred non-estrus. Pregnancy was determined by rectal palpation. There were no significant differences between breeding systems for total pregnancy (TP), total AI pregnancy (AIP) or AI first service pregnancy rates. The average day of conception for the $PGF_{2\alpha}$ system (day 20) was significantly closer ($P<.01$) to the start of the breeding season than the conventional system (day 23). In the second study, two trials were conducted using heifers in trial 1 and lactating cows in trial 2. Animals in both trials were assigned to one of three treatments. Treatment one was non-treated controls and were bred for 45 days natural service. Treatment two received two injections of 15 mg $PGF_{2\alpha}$ (IM) and treatment three received two injections of 25 mg $PGF_{2\alpha}$ (IM) 11 days apart. Cattle in treatments 2 and 3 were bred about 74 hours post the second $PGF_{2\alpha}$ injection without regard to estrus. Approximately 48 hours after insemination $PGF_{2\alpha}$ treated cattle were exposed to natural breeding for 18 days. On day 21 of the breeding season bulls were removed and estrus detection commenced. AI resumed on day 22 and continued until day 26 of the breeding season at which time natural service resumed until day 45 of the breeding season. TP rates were determined by rectal palpation. There were no significant differences between treatments 1,2 and 3 for TP. Study three analyzed breeding trials conducted during fall 1974(F74), summer 1975(S75), fall 1975(F75) and summer 1976(S76) to test the effect of $PGF_{2\alpha}$ on fertility when administered for 2 years to the same cattle. Methods and materials for this study are similar to study one in all respects except for the F74 nonestrus breeding which occurred at 72 hrs post $PGF_{2\alpha}$ treatment. TP and AIP rates were not different between breeding systems after year 1; however TP and AIP rates were greater ($P=.035$ and $P=.006$, respectively) in the $PGF_{2\alpha}$ system after year 2. In the conventional system TP and AIP rates decreased ($P<.001$) from year 1 to year 2. Similar trends were observed in the $PGF_{2\alpha}$ system for TP($P=.001$) and AIP($P>.10$) from year 1 to year 2.

CHAPTER 1

INTRODUCTION

In order to increase the quantity and quality of beef produced many beef producers have looked to artifical insemination for the following reasons;

1. Utilization of superior sires for rapid genetic improvement.
2. Facilitation of cross-breeding schemes.
3. Protection against venereal disease.

Under present day management schemes, artifical insemination (AI) has been shown to be comparable to natural service on a cost per calf basis, (Syntex Corporation, 1975; Moore, 1974; Stevens and Mohr, 1969).

During the last decade many estrus synchronizing agents have been studied. A successful estrus synchronizing agent for beef cattle would facilitate artifical insemination for many producers. With estrus control, producers could inseminate a larger number of cows in a shorter period of time thus reducing labor requirements for an AI breeding program. Because of the shorter breeding season a shorter calving season would result. A shorter calving season would reduce the age variation between calves at weaning thus a producer could have a more uniform product to market.

The main objectives of this study was to evaluate fertility

after Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) controlled estrus and the practical application of management systems utilizing $PGF_{2\alpha}$ under range beef production conditions.

CHAPTER 2

LITERATURE REVIEW

2.1. General Endrocrinology of the Bovine Estrous Cycle

The hormonal interrelationships which are responsible for regulation of the estrous cycle in the cow are very complex. Figure 1 illustrates the relationship between the pituitary gland, hypothalmus, ovaries and uterus in the cycling bovine. The hypothalmus secretes gonadotropic relasing hormones (GnRH) into the hypothalmic-hypophyseal portal system which causes the release of follicle stimulating hormone (FSH), and lutenizing hormone (LH) (Figure 1) from the adenohypophysis (Niswender et al. 1974).

FSH is responsible for the early maturation of ovarian follicles (Ganong, 1975; Schwartz, 1974). FSH and LH together are responsible for the final maturation of the ovarian follicle and ovulation. LH and FSH act synergistically to cause the production and secretion of estrogen by the follicle. Increasing levels of estrogen during the maturation of the ovarian follicles exerts a feedback (Figure 1) on the hypothalamo-hypophyseal axis causing the release of peak levels of LH and FSH (Niswender et al. 1974). Ovulation in the bovine occurs from 25 to 30 hours after LH reaches its peak level (Foote, 1974). There is little evidence that prolactin plays an important luteotropic or luteolytic role in any of the domestic animals (Hansel et al. 1973). After ovulation the levels of gonadtropins and estrogen are greatly reduced and the level of progesterone is increased. LH at this reduced

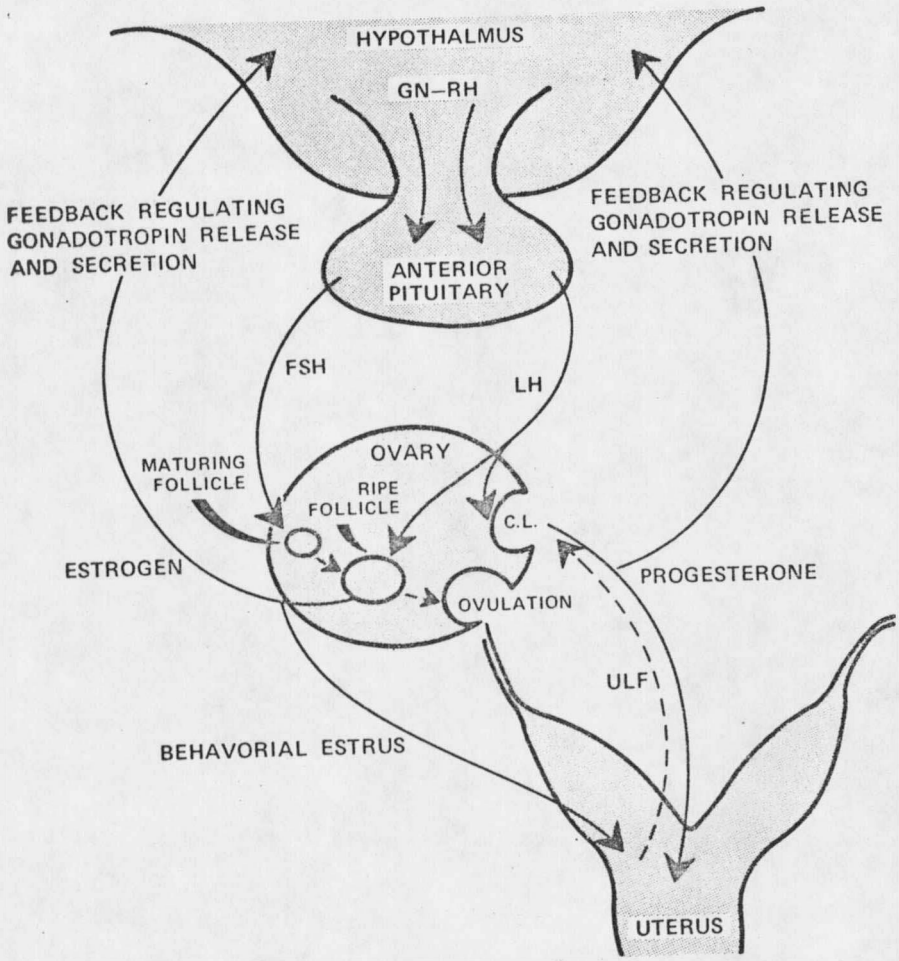

FIGURE 1. PRINCIPLE ENDOCRINE PATHWAYS INVOLVED IN THE CONTROL OF OVARIAN FUNCTION

level is partially responsible for the mitotic proliferation of granulosa cells from the ruptered follicle into luteal cells, which secrete progesterone and form the corpus luteium (CL). Progesterone prepares the uterus for acceptance of the fertilized ova (Niswender et al. 1974).

At about day 16 of a 21 day bovine cycle the CL will begin to regress in a non-pregnant cow causing a decrease in progesterone (Hansel et al. 1973). Regression of the CL or luteolysis in this review is defined as a net loss of total luteal cell numbers, and a decrease in progesterone secretion. Following CL regression more follicles will mature and estrogen will again predominate over progesterone. The cycle may be thought of in terms of an alteration in the dominance of progesterone and estrogen, both ovarian steroid hormones (Perry 1971). Ovarian steroid homrones exert feedback on the pituitary hypothalmic axis and regulate secretion and release of gonadotripins which regulate follicular maturation, estrogen production and ovulation.

On day 12 or 13 of the ovine estrous cycle the uterus has been shown to impose its luteolytic effect and initiate a new estrous cycle. In the pregnant animal the conceptus maintains the CL by neutralizing the luteolytic factor secreted from the uterus (Caldwell et al. 1969).

2.2. The Uterine Luteolytic Factor (ULF)

2.2.1 ULF History

Since early work by Loeb (1923) much interest has been shown in the field of uterine control of the life span of the corpus luteum. Loeb reported that in the non-pregnant guinea pig, total or almost total hysterectomy is followed by prolonged corpora lutea for 60 to 80 days. In later years Loeb suggested that prolongation of the CL during pregnancy was due to functional inactivation of the uterine mucosa under the influence of the developing embryo and placenta. Hechter et al. (1940) implied that the uterus may produce a hormone which causes the CL to regress and in the absence of this hormone the CL are maintained.

2.2.2. ULF Origin

Investigations by Wiltbank and Casida (1956) revealed that hysterectomy prolonged the life span of the CL past the normal time of regression in the ewe and cow. They also reported that removal of half of the uterus in the ewe did not extend the life span of the CL however, partial removal of the uterus in the cow increased the life of the CL. Later experiments by LaVoie et al. (1975) and Stellflug et al. (1975 a) using hysterectomized bovine demonstrated that the uterus is implicated in luteolysis. Estrous cycles, CL size and progesterone content for hysterectomized cows were similar to mid cycle

intact animals.

Further evidence to support the theory that the luteolysin is produced by the endometrium of the uterus and that the luteolysin could be $PGF_{2\alpha}$ was presented by Oxender (1974). Dilute iodine solution (DIS) was infused in the uterus of cows on day 4 or day 15 of the estrous cycle. The DIS rapdily destroyed the endometrium and it did not regenerate for 4 or 5 days. When DIS was infused on day 4, the estrous cycle was shortened and when DIS was infused on day 15, the estrous cycle was lengthened to 25 days. When DIS was infused on day 15 and $PGF_{2\alpha}$ was infused on day 16 the estrous cycle was reduced from 25.1 to 19.1 days. The results of this experiment indicate that the luteolysin is produced by the endometrium of the uterus.

2.2.3. Localized Effect of the ULF

Evidence indicates that the uterine luteolytic effect in the cow is local and depends on the presence of the uterine horn ispilateral to the CL (Hansel et al. 1973). Ispilateral regression of the CL has been observed in partially hysterectomized sows (du Mesnil du Buisson, 1961) and ewes (Inskeep and Butcher, 1966).

Hansel and co-workers (1973) reported that when the ovary containing the active CL was surgically isolated from all nerve and circulatory ties with the uterus on day 10-12 of the bovine cycle, the CL were maintained in 4 of 5 animals as indicated by weights and

progesterone concentrations obtained at the time of their removal 30-36 days postsurgery. None of the experimental animals exhibited estrus during this period.

Ovarian transplant experiments have exhibited some of the most impressive evidence for a local luteolytic role of the uterus in the ewe and cow. Ewes with ovaries transplanted to the neck, did not undergo regular estrous cycles and the progesterone content of ovarian effluent blood remained high for long periods of time (McCracken et al. 1971). Hansel and Snook (1970) observed irregular estrous cycles in one cow in which the ovary was transplanted to the neck for over one year.

From the evidence cited, it is obvious that the uterus secretes a substance that is responsible for luteolysis and that the ovary and uterus must be in close proximitiy for luteal regression to occur normally. For pregnancy to be maintained, the corpus luteum must be functional until the placenta is capable of producing adequate progesterone to maintain pregnancy. Thus, the life span of a corpus luteum is of considerable importance since it regulates the length of the estrous cycle and is essential for maintenance of pregnancy.

2.2.4 Embryo Effect on the Luteolytic Process

A sequence of investigations by Moor and Rowson (1966 a,b,c,d) were performed to determine the time at which the embryo exerts its

influence on the luteolytic process. The transfer of embryos to non-pregnant ewes throughout the estrous cycle indicated that the embryo must be in the uterus by day 12 or 13 in order to extend the life span of the CL thus neutralizing the ULF. The removal of embryos from pregnant ewes confirmed these results.

2.3. The Relationship of $PGF_{2\alpha}$ to the Uterine Luteolytic Factor

Many observations clearly indicate that the uterus produces a substance which causes luteolysis in the bovine (Hansel et al. 1973; Melampy and Anderson, 1968; Lukaszewaska and Hansel, 1970). During a group discussion in 1966, Babcock first suggested that prostaglandins might be the uterine luteolytic factor.

Pharriss and Wyngarden (1969) indicated that prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) caused the CL to regress in rats. $PGF_{2\alpha}$ has since been reported to be luteolytic in guinea pigs (Blatchley and Donovan, 1969), rabbits (Pharriss, 1970), sheep (McCracken, Glew and Scaramuzzi, 1970), hamsters (Lauderdale, 1972; Gutknecth, Wyngarden and Pharriss, 1971; Laphsetwar, 1971), cows (Rowson, Tervit, and Brand, 1972; Inskeep, 1973; LaVoie, 1975) and horses (Douglas and Ginther, 1972; Allen, 1972).

2.3.1. General Description and Origin of Prostaglandins

Prostaglandins were discovered in the 1930's (Goldblott, 1933; Von Euler, 1934) and have since been associated with the reproductive processes in many mammalian species. Prostaglandins are 20-carbon

hydroxy fatty acids with a cycleopentane ring and two side-chains. Prostaglandins are divided into four groups (E, F, A and B), indicating differences in the five-membered cyclopentane ring. Precursors for the biosynthesis of prostaglandins are 8, 11, 14-Eicosatetranoic acid, arachidonic acid and 5,8, 11, 14, 17-Eicosapentaneoic acid. These precursor acids are derived from linoleic acid (Karim, 1975). Prostaglandins have been isolated or released from lung, thymus, brain, spinal cord, kidney, iris, umbilical cord, endometrium over ova, fat, adrenals, ovaries, stomach, intestines, nerves, menstrual fluid, amniotic fluid, seminal plasma, blood, skeletal muscle, cardiac muscle, salivary glands, thyroid, pancreas, and uterus (Bergstrom et al. 1968).

2.3.2. Postulated Mechanisms of $PGF_{2\alpha}$ Induced Luteolysis

The mechanism in which $PGF_{2\alpha}$ exerts its luteolytic effect is unknown. Pharris et al. (1972) postulates five possible modes of action by which $PGF_{2\alpha}$ may cause luteolysis. Figure 2 depicts the five postulated areas where $PGF_{2\alpha}$ could be exerting its primary effect.

Postulate one states $PGF_{2\alpha}$ either totally blocks the pituitary or has the ability to suppress the secretion of the luteotropic complex in different species (Figure 2, #1). If $PGF_{2\alpha}$ directed its luteolytic effect through the hypotholmus or pituitary then luteolysis should occur throughout the entire estrous cycle. Numerous investigations have found that $PGF_{2\alpha}$ is only effective in causing luteolysis