



Comparison of breeding management systems using either one or two injections of PGF α 2a in suckled beef cows

by Gail Milton Vennes

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

Montana State University

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Abstract:

Three herds of suckled beef cows (2 to 10 years old; n=656), at least 50 days post-partum, were used in two trials. In trial 1, members within a herd were assigned randomly to three groups: 1) controls, artificially inseminated (AI) 12 hr after detected estrus; 2) cows receiving two injections of 25 mg PGF α 2a (free acid equivalent) 11 days apart followed by AI 12 hr after detected estrus until 80 hr post-treatment at which time all members not yet bred were inseminated (LL-AI-E-80); and 3) cows receiving the same PGF α 2a treatment as LL-AI-E-80 but inseminated only at 80 hr post-treatment (appointment bred) (LL-AI-80). Observations of all groups for estrus began immediately after the second PGF α 2a injection and were made twice daily for a 6-day period. PGF α 2a-treated cows, which were detected in estrus after day 4 were reinseminated utilizing a genetic marker to determine sire of calf. Clean-up bulls were introduced 12 hr after the last AI for the remainder of a 50-day breeding season. The rate of detected estrus during the first 4 days of detection was significantly higher ($P < .05$) in the PGF α 2a-treated cows than in the controls. Cumulative AI pregnancy rates (no. pregnant - no. in group) by day 4 of breeding were: 12, 45 and 39% for controls, LL-AI-E-80 and LL-AI-80, respectively; the percent pregnant for LL-AI-E-80 and LL-AI-80 was higher ($P < .05$) than controls but did not differ ($P > .05$) from each other. Total pregnancy rates of cows detected (no. pregnant - no. detected) in 4 days were not different ($P > .05$) among groups. Thirty-nine percent of the PGF α 2a-treated cows that were not detected in estrus during the 6 days post-treatment were pregnant from the 80 hr breeding; none of those detected on days 5 or 6 were pregnant to this breeding. In trial 2, controls in trial 1 from two herds (n=14) were injected with PGF α 2a if they had not been detected in estrus by day 4.5 and AI was continued for 4 more days (AI-L-AI-E). Reproductive performance of this group was compared with that of their LL-AI-80 herdmates (n=109). First AI pregnancy rates (no. pregnant to 1st AI - no. inseminated) were 68 and 47% ($P > .05$) for AI-L-AI-E and LL-AI-80, respectively. Total AI pregnancy rates (no. pregnant to 1st AI - no. in group) were 54 and 47% ($P > .05$) for AI-L-AI-E and LL-AI-80, respectively. Cumulative calving rates (no. calved - no. in group) by day of calving season for AI-L-AI-E and LL-AI-80, respectively, were day 10, 60 and 64%; day 38, 75 and 89% ($P < .05$) and day 60, 87 and 93%. Time of onset of estrus up to 96 hr after the double PGF α 2a injection system did not influence pregnancy rate to an 80 hr breeding. The number of AI calves produced in either the AI-L-AI-E or LL-AI-80 system did not differ, but more calves were born in the first 38 days of calving after the LL-AI-80 plus clean-up bull system than after the AI-L-AI-E plus clean-up bull system.

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Date March 17, 1982

COMPARISON OF BREEDING MANAGEMENT SYSTEMS USING EITHER
ONE OR TWO INJECTIONS OF PGF_{2α} IN SUCKLED BEEF COWS

by

GAIL MILTON VENNES

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

of

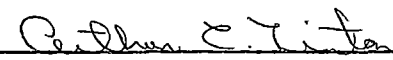
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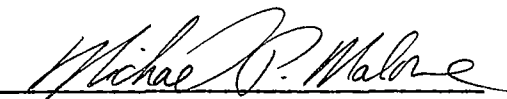
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ABSTRACT

Three herds of suckled beef cows (2 to 10 years old; n=656), at least 50 days post-partum, were used in two trials. In trial 1, members within a herd were assigned randomly to three groups: 1) controls, artificially inseminated (AI) 12 hr after detected estrus; 2) cows receiving two injections of 25 mg $\text{PGF}_{2\alpha}$ (free acid equivalent) 11 days apart followed by AI 12 hr after detected estrus until 80 hr post-treatment at which time all members not yet bred were inseminated (LL-AI-E-80); and 3) cows receiving the same $\text{PGF}_{2\alpha}$ treatment as LL-AI-E-80 but inseminated only at 80 hr post-treatment (appointment bred) (LL-AI-80). Observations of all groups for estrus began immediately after the second $\text{PGF}_{2\alpha}$ injection and were made twice daily for a 6-day period. $\text{PGF}_{2\alpha}$ -treated cows, which were detected in estrus after day 4 were reinseminated utilizing a genetic marker to determine sire of calf. Clean-up bulls were introduced 12 hr after the last AI for the remainder of a 50-day breeding season. The rate of detected estrus during the first 4 days of detection was significantly higher ($P<.05$) in the $\text{PGF}_{2\alpha}$ -treated cows than in the controls. Cumulative AI pregnancy rates (no. pregnant - no. in group) by day 4 of breeding were: 12, 45 and 39% for controls, LL-AI-E-80 and LL-AI-80, respectively; the percent pregnant for LL-AI-E-80 and LL-AI-80 was higher ($P<.05$) than controls but did not differ ($P>.05$) from each other. Total pregnancy rates of cows detected (no. pregnant - no. detected) in 4 days were not different ($P>.05$) among groups. Thirty-nine percent of the $\text{PGF}_{2\alpha}$ -treated cows that were not detected in estrus during the 6 days post-treatment were pregnant from the 80 hr breeding; none of those detected on days 5 or 6 were pregnant to this breeding. In trial 2, controls in trial 1 from two herds (n=114) were injected with $\text{PGF}_{2\alpha}$ if they had not been detected in estrus by day 4.5 and AI was continued for 4 more days (AI-L-AI-E). Reproductive performance of this group was compared with that of their LL-AI-80 herdmates (n=109). First AI pregnancy rates (no. pregnant to 1st AI - no. inseminated) were 68 and 47% ($P<.05$) for AI-L-AI-E and LL-AI-80, respectively. Total AI pregnancy rates (no. pregnant to 1st AI - no. in group) were 54 and 47% ($P>.05$) for AI-L-AI-E and LL-AI-80, respectively. Cumulative calving rates (no. calved - no. in group) by day of calving season for AI-L-AI-E and LL-AI-80, respectively, were day 10, 60 and 64%; day 38, 75 and 89% ($P<.05$) and day 60, 87 and 93%. Time of onset of estrus up to 96 hr after the double $\text{PGF}_{2\alpha}$ injection system did not influence pregnancy rate to an 80 hr breeding. The number of AI calves produced in either the AI-L-AI-E or LL-AI-80 system did not differ, but more calves were born in the first 38 days of calving after the LL-AI-80 plus clean-up bull system than after the AI-L-AI-E plus clean-up bull system.

INTRODUCTION

Interest in the development of methods to control the estrous cycle of the bovine has evolved from the possibility that one could manipulate a group of females so they would be at the same stage of the cycle at a specific time for breeding. This would allow producers to utilize artificial insemination (AI) without needing additional pasture, facilities and time required for detecting estrus (heat) in a group of randomly cycling females for up to 25 days to get them bred. Artificial insemination is an appealing management tool for improving the genetic potential within a herd because it provides access to proven sires which may not otherwise be available because of economic or geographical constraints. Artificial insemination has been widely accepted in the dairy industry and has resulted in extensive genetic and phenotypic progress in individual milk production. But, dairy producers are not labored with the extra time for heat detection because their production animals are always available during normal routine, and AI can be incorporated readily into dairy breeding programs. The use of AI in breeding programs for dairy replacement heifers and beef cattle has not been accepted easily. Yet, the desire of producers to utilize AI in these animals still exists.

Beef and dairy producers in the United States have been provided the opportunity to use estrous synchronization in breeding programs because of the release of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) by the Food and

Drug Administration (FDA). This drug is approved for use in dairy heifers and all classes of beef females. Prostaglandin $F_{2\alpha}$ is a naturally occurring substance that will effectively shorten the estrous cycle when administered during the luteal phase. Therefore, the interval of estrus in a group of randomly cycling cows may be "synchronized" with the use of this product. Breeding systems recommended for use following administration of $PGF_{2\alpha}$ include: 1) AI either after detected estrus or at 80 hr following two injections, 10 to 12 days apart; 2) AI after detected estrus following a single injection; or 3) natural service.

To implement the use of $PGF_{2\alpha}$ in a breeding management system for range beef cattle, it is necessary to understand the bovine estrous cycle and the mechanisms involved in its regulation. Therefore, the following review of literature will be presented that describes the estrous cycle in the bovine and its controlling mechanisms. Alternative methods for estrous synchronization will also be covered, and the advantages and disadvantages of these methods will be compared with those that incorporate $PGF_{2\alpha}$.

REVIEW OF LITERATURE

The Bovine Estrous Cycle

Events of the mature female bovine reproductive system occur in a symmetrical pattern called the estrous cycle (Sorenson, 1979). The normal estrous cycle has an average length of 20 to 21 days and is usually only interrupted by pregnancy. Various cyclic changes occur in the reproductive organs of the female bovine during the estrous cycle. These changes are reflective of both morphological and physiological events that occur in the ovary and reproductive tract and are thought to be regulated by interactions between the neuroendocrine (hypothalamus) and reproductive endocrine systems (pituitary and ovaries). These interactions are characterized by feedback control mechanisms involving the hypothalamic-pituitary-ovarian axis (see review by Niswender et al., 1974). The following discussion on divisions of the estrous cycle are based on cyclic ovarian and behavioral changes.

Divisions of the Estrous Cycle.

Four major divisions of the estrous cycle can be discerned and they are: 1) estrus, 2) metestrus, 3) diestrus and 4) proestrus.

Estrus marks the beginning of the cycle and is usually designated day 0. Sorenson (1979) defined estrus as the period of desire or time when the female will accept the male for mating. This period lasts for approximately 16 hours but may range from 12 to 24 hours

(Robinson, 1977). During this period at least one of the ovaries contains a large, mature follicle which will ovulate about 10 hours after the end of estrus (Robinson, 1977) or 24 to 32 hours after the onset of estrus (Manns and Hafs, 1976).

Metestrus begins immediately following estrus and is usually two days in length (days 2-4). The major ovarian event of metestrus is ovulation or release of the ova from the ovary. The cellular and biochemical events in the ovulatory process have been reviewed by Espey (1974) and will not be discussed in this text. Following ovulation, the proliferating granulosa and theca interna cells of the ruptured follicle differentiate into luteal cells to form the corpus hemorrhagicum. This structure matures to eventually form a corpus luteum (CL) in the next stage.

Diestrus is characterized by the presence of the definitive CL in the ovary. Length of diestrus is variable but usually lasts approximately 11 days (days 5-16). If fertilization and conception from mating during estrus have not occurred regression of the CL (luteolysis) is initiated on day 16 (Stabenfeldt et al., 1978). It has been noted that follicular growth occurs during diestrus (Stabenfeldt et al., 1980), however these follicles do not usually mature but undergo atresia (follicular death). It may be that follicular growth during this period is one factor in the initiation of luteolysis.

If luteolysis is initiated diestrus ends and proestrus (days 17-20) begins. During this period luteolysis is completed and a corpus albicans is the result of this process. Extensive follicular growth takes place during proestrus, and the follicle(s) destined to ovulate becomes developed for ovulation after the subsequent estrus (Stabenfeldt et al., 1978).

Hormonal Control of the Estrous Cycle.

The major hormones involved in regulation of the estrous cycle are: follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary; progesterone (P_4) from the CL; estrogens (mainly estradiol-17 β ; E_2) from ovarian follicles; and gonadotropin releasing hormone (GnRH) from the hypothalamus. Prostaglandin $F_{2\alpha}$, although not considered a hormone per se, is another important effector that is produced by the endometrium of the uterus.

The pituitary gonadotropins, FSH and LH, are necessary for growth and maturation of the follicle and ovulation (Sorenson, 1979). Plasma concentration patterns of the gonadotropins show low tonic levels through most of the cycle until after luteolysis. There are slight increases, mainly on day 10, which are thought to be involved in midcycle follicular growth. These increases are short in duration and concentrations immediately return to basal levels (Robinson, 1977). During proestrus plasma FSH concentrations begin to rise shortly after

luteolysis to peak levels at or near the onset of estrus then decline rapidly (Hackett and Hafs, 1969). Plasma LH concentrations "surge" from 2-3 ng/ml up to 10-50 ng/ml near the onset of estrus, remain elevated for 8-10 hours, then rapidly decline (Stabenfeldt *et al.*, 1978). The LH surge is a major stimulus for ovulation (Espey, 1974), and low basal concentrations of LH that follow in metestrus are necessary for the formation and maintenance of the CL (Hansel *et al.*, 1973).

Plasma concentrations of the ovarian hormones, P_4 and estrogens, fluctuate relative to the activity of their respective secretory ovarian structure. Progesterone, secreted primarily by the corpus luteum, rises from <1 ng/ml to 6-7 ng/ml between days 5 and 10 during diestrus (Smith *et al.*, 1975) and remain elevated until day 16 when luteolysis is initiated (Catchpole, 1977). One of the major functions of progesterone is physiological preparation of the uterus for pregnancy, if it occurs (Sorenson, 1979). Plasma E_2 concentrations increase during diestrus when follicular growth is activated but subside as atresia occurs (Smith *et al.*, 1975). The major peak of E_2 concentrations (7-11 pg/ml) occurs about one day prior to estrus and is the major stimulus for the preovulatory LH surge (Chenault *et al.*, 1975) and inducing behavioral estrus (Ganong, 1977). Injections of E_2 resulted in inducing behavioral estrus in ovariectomized heifers (Carrick and Shelton, 1969) and a preovulatory-like LH surge in

prepubertal heifers (Schillo et al., 1981). Estrogens produced during diestrus may initiate the release of $\text{PGF}_{2\alpha}$ from the uterus to cause luteolysis (Goldberg and Ramwell, 1975).

Release patterns of $\text{PGF}_{2\alpha}$ into the uterine vein have been determined by measuring plasma concentrations of 13,14-dihydro-15-keto- $\text{PGF}_{2\alpha}$, the major metabolite of $\text{PGF}_{2\alpha}$ (Peterson et al., 1975). Well defined surges of this $\text{PGF}_{2\alpha}$ metabolite of about six hours duration occur beginning on day 16, with total luteolysis occurring in about 36 hours (Stabenfeldt et al., 1980).

The hypothalamus produces and releases GnRH which regulates the release of both FSH and LH from the anterior pituitary. The hypothalamus is thought to be the regulatory center both for tonic and episodic release of the gonadotropins (Lamming et al., 1979). The tonic and episodic release centers are controlled by negative feedback effects of P_4 and E_2 . Thus, as the plasma concentrations of these ovarian hormones increase, an inhibition of GnRH release results. Yet, in the ewe with respect to LH release, P_4 acts on the hypothalamus to decrease the frequency of GnRH discharges while E_2 acts in the pituitary to decrease its response to each GnRH pulse (Goodman and Karsch, 1980). These authors suggested that this is also the situation in the cow. The preovulatory LH surge is triggered through a positive feedback of E_2 acting primarily on the surge center in the hypothalamus and secondarily at the level of the pituitary (Lamming et

al., 1979).

With the basic understanding of the morphological and physiological changes that occur during the bovine estrous cycle and the neuroendocrine and endocrine hormones that regulate these changes it is possible to conclude that one might manipulate the estrous cycle hormonally so as to control the time of estrus and ovulation in the female bovine.

Control of Estrus and Ovulation

Use of Progesterone and Progestagens.

Mechanism of control. It is hypothesized that progesterone inhibits the release of GnRH from the hypothalamus which regulates the release of gonadotropins from the pituitary. Therefore, when plasma progesterone levels are high, growth and maturation of follicles, estrus and ovulation are inhibited. Thus, by treating a group of randomly cycling bovine females with exogenous progesterone or progestagens for at least 16 days (the length of the cycle through diestrus) all animals would be in proestrus when treatment is withdrawn and synchronized estrus and ovulation would follow.

Types of progesterone. Suspensions of P_4 in corn oil were first used in progesterone treatment regimens. Orally active progestagens were developed in work on human contraception and this generated interest in feeding these progestagens to cattle. These compounds

include: 6-methyl-17-acetoxypregesterne (MAP), 6-chloro-6-dehydro-17-acetoxypregesterone (CAP), dihydroxypregesterone acetophenide (DHPA) and melengestrol acetate (MGA) and can be mixed with feed concentrates or water for administration. Other types of progestagens have been developed and incorporated into intravaginal devices and subcutaneous implants. These include: 17 α -acetoxy-9-fluro-11 β -hydroxypregesterone (Cronolone[®], SC-9880), 17 α -ethyl-19-nortestosterone (Nilevar[®], SC-5914) and 17 α -acetoxy-11 β -19-norpregesterone (Norgestamet[®], SC-21009).

Methods of administration. Daily injections of 50 mg P₄ for 13 to 17 days or a single injection of 560 mg P₄ are effective in suppressing heat and preventing ovulation in bovine females (Christian and Casida, 1948; Willett, 1950; Ulberg et al., 1951; Trimberger and Hansel, 1955; Nellor and Cole, 1956). Studies on fertility in bovine females inseminated at the estrus after these treatments showed lower than normal fertility (Willett, 1950, Trimberger and Hansel, 1955; Nellor and Cole, 1956). But, fertility at the second post-treatment estrus was normal (Hansel et al., 1959; Osland et al., 1970). Ray et al. (1961) studied the physiological and morphological effects of exogenous P₄ on the bovine female reproductive tract. These effects included: lowered pituitary FSH and LH potencies; smaller CL diameters; and lower cell heights of glandular endometrial epithelium.

It was suggested that these effects contributed to the lowered fertility after P_4 treatment.

The use of more stable orally-active progestagens was studied as an alternate route of administering P_4 to bovine females. Successful inhibition of estrus and ovulation was reported after feeding MAP for 11 to 20 days (Hansel and Malven, 1960; Hansel et al., 1961; Collins et al., 1961; Nelms and Combs, 1961; Zimbelman, 1961; Anderson et al., 1962; Fahning et al., 1966). A more potent progestagen, CAP, was less effective in synchronizing estrus when fed for the same length of time (Van Blake et al., 1961; Hansel et al., 1966; Wagner et al., 1968). But, successful synchronization of estrus occurred after feeding an even more potent progestagen, MGA (Zimbelman and Smith, 1966; Roussel and Beatty, 1969; Roussel et al., 1969; Hill et al., 1971). Also DHPA effectively synchronized estrus in beef heifers when fed for 20 days (Wilbank et al., 1967). Fertility to inseminations at the estrus after cessation of treatment with these progestagens was always at least 10 to 15 percent lower than that in untreated controls (Hansel et al., 1966; Wiltbank et al., 1967, Roussel et al., 1969, Hill et al., 1971).

Due to the inability to precisely control the amount of progestagen intake by individuals in a group of animals fed progestagens, intravaginal and subcutaneous implants were studied as another method of administration. Cronolone-impregnated sponge

pessaries placed intravaginally in bovine females for 18 or 19 days were effective in synchronizing estrus and ovulation (Carrick and Shelton, 1967; Shimizu *et al.*, 1967; Wishart and Hoskin, 1968). Retention of these pessaries through the treatment period was less than satisfactory, but this was remedied by applying antibiotics prior to insertion (Scanlon *et al.*, 1972). Roche (1976a) reported satisfactory retention and synchronization of estrus in bovine females receiving a silastic coil progesterone-releasing-intravaginal-device (PRID) for 12 days. Successful synchronization of estrus in cows receiving either MAP-impregnated subcutaneous rubber implants for 22 to 64 days or plastic subcutaneous Nilevar implants for 16 days was reported by Dzuik *et al.* (1966) and Curl *et al.* (1968), respectively. Although these methods of administration did improve the regulation of progesterone or progestagen intake the problem of low fertility at the estrus after removal of the source still persisted.

Since progesterone and progestagen treatments were undesirable because of low fertility other methods to control estrus and ovulation were needed. With the development of a partial understanding of the mechanism of luteolysis during the estrous cycle, the use of exogenous luteolytic agents has been studied as an alternative method of control.

Use of Luteolytic Agents.

Mechanism of luteolysis. It has been established that the uterus is necessary for initiating luteolysis in the bovine. Wiltbank and Casida (1956) reported that removal of the uterus (hysterectomy) prolonged normal CL function in the nonpregnant cow. From this and similar work in other mammals it was hypothesized that the uterus produced a substance that caused regression of the CL. Through the use of auto-transplants of ovaries and uteri in ewes (McCracken *et al.*, 1972) and partial hysterectomies in cows and ewes (Cumming, 1975) it was established that the effect of the uterus on the CL is local in nature and required the uterine horn ipsilateral to the ovary containing the CL.

Phariss and Wyngarden (1969) suggested that a prostaglandin might be the uterine-produced substance that caused luteolysis. They showed that prostaglandin $F_{2\alpha}$ is found in abundance in the uterus and high doses administered to rats (1 mg/kg/day) caused a significant shortening of pseudopregnancy. Babcock (1966) had first suggested that prostaglandins might be luteolytic and this was culminated by research done by McCracken *et al.* (1972) in the ewe (as reviewed by Hansel *et al.*, 1973). Their conclusion was based on: 1) infusion of $PGF_{2\alpha}$ at a level of 25 ug/hr into the arterial supply of the auto-transplanted ovary (in the neck area) caused a rapid decline in progesterone secretion, followed by a rise in estradiol secretion and

a peak in LH secretion which occurred shortly after the onset of estrus; 2) the level of $\text{PGF}_{2\alpha}$ in the uterine venous blood of the ewe increases at about the same time the CL begins to regress; and 3) peak levels of $\text{PGF}_{2\alpha}$ of 42 ng/ml of uterine vein plasma have been measured. Assuming a uterine vein blood flow of 15 ml/min, it may be calculated that the uterus can release up to 25 ug/hr of $\text{PGF}_{2\alpha}$. Infusion of $\text{PGF}_{2\alpha}$ at this rate into the uterine vein has been shown to cause premature luteolysis and a decline in plasma progesterone in three intact ewes treated on days 6, 10 and 14 (luteal phase) of the cycle. Hansel et al. (1973) refuted this conclusion in reference to the bovine by citing evidence that $\text{PGF}_{2\alpha}$ and other prostaglandins were luteotropic when added to bovine luteal tissue in vitro.

With the idea that $\text{PGF}_{2\alpha}$ could be the endogenous uterine luteolysin, attempts to induce luteolysis with exogenous $\text{PGF}_{2\alpha}$ were performed. Successful CL regression was attained in cattle using intra-uterine infusions (Liehr et al., 1972; Rowson et al., 1972; Lamond et al., 1973; Louis et al., 1974), subcutaneous injections (Lauderdale, 1972) and intramuscular injections (Stellflug et al., 1975). Support for the conclusion that $\text{PGF}_{2\alpha}$ is the endogenous uterine luteolysin in the bovine has been provided by measurement of this substance in the uterine endometrium, uterine vein and ovarian artery. Shemish and Hansel (1975) and Lamothe et al. (1977) reported cyclic variations in uterine secretions of $\text{PGF}_{2\alpha}$ with highest values

being observed during luteal regression. LaVoie et al. (1975) further supported this conclusion by demonstrating that CL regression could be induced in totally hysterectomized cows with single injections of 30 mg $\text{PGF}_{2\alpha}$.

It has been determined that a local utero-ovarian pathway is involved in uterine induced luteolysis in the bovine (as reviewed by Ginther, 1974). The nature of this pathway has been hypothesized to involve the close apposition of the utero-ovarian vein with the ovarian artery. This allows for a "counter current" mechanism where by $\text{PGF}_{2\alpha}$ from uterine venous blood is passed through the wall of the utero-ovarian vein into the ovarian blood supply. This allows the transfer to occur without entering the systemic circulation. McCracken et al. (1972) reported that in ewes, tritium labelled $\text{PGF}_{2\alpha}$ infusion into the utero-ovarian vein was followed by a higher concentration of labelled $\text{PGF}_{2\alpha}$ being detected in the ipsilateral ovarian artery than that detected in the iliac artery. This supports the counter current exchange concept.

Further attempts to support this concept in reference to the cow have been questioned due to failure to observe increased concentrations of $\text{PGF}_{2\alpha}$ in ovarian arterial blood at times when concentrations of $\text{PGF}_{2\alpha}$ in uterine venous plasma were clearly elevated (Inskeep and Murdoch, 1980). Hansel et al. (1976) pointed out that problems in measuring plasma $\text{PGF}_{2\alpha}$ are encountered due to wide

distribution of prostaglandin synthetase in many tissues. These workers cited evidence that mechanical manipulation of the reproductive tract and even saline injections into ovaries can elevate $\text{PGF}_{2\alpha}$ concentrations. To further confound the problem of determination of $\text{PGF}_{2\alpha}$ in blood it was noted that blood platelets produce prostaglandins in the clotting process although this can be remedied by rapid centrifugation and freezing following blood withdrawal. Yet, it is apparent that the significance of plasma prostaglandin concentrations is debatable.

It has been hypothesized that progesterone and estrogen play a key role in stimulating $\text{PGF}_{2\alpha}$ synthesis in the uterus. Stabenfeldt et al. (1980) reviewed evidence that estrogens are necessary for the synthesis of enzymes needed to either hydrolyze the phospholipid source of arachidonic acid, the precursor of $\text{PGF}_{2\alpha}$, or synthesize $\text{PGF}_{2\alpha}$. Also, it was hypothesized that exposure of the uterus to progesterone was necessary for developing the lipid droplets which contain the phospholipids. This may help to explain why single injections of $\text{PGF}_{2\alpha}$ are not effective on cycling cows that are in the metestrus stage (Rowson et al., 1972; Henricks et al., 1974). The uterus has not received ample exposure to P_4 during metestrus. However, Beal et al. (1980) reported successful inhibition of progesterone secretion by CL in Holstein heifers that were in days 3 and 4 of their cycle with twice daily intramuscular injections of 25

mg $\text{PGF}_{2\alpha}$.

The precise mechanism by which $\text{PGF}_{2\alpha}$ causes demise of luteal tissue has not been reported unequivocally. Many hypotheses have been presented but most of these have been refuted.

Henderson and McNatty (1975) have hypothesized a plausible biochemical mechanism of $\text{PGF}_{2\alpha}$ -induced luteolysis. These workers cited evidence that explained the mechanism of progesterone production of the luteal cell. The plasma membrane of luteal cells contain specific binding sites for LH which, upon reception of LH, activate the adenyl cyclase system necessary for activation of the steroidogenic enzymes. Following the preovulatory LH surge, these receptor sites become activated; this results in morphological and functional (progesterone production) luteinization. The plasma membrane of luteal cells also contain specific binding sites for $\text{PGF}_{2\alpha}$ (Kimball and Lauderdale, 1975) but when LH has filled its membrane receptors these sites are masked for $\text{PGF}_{2\alpha}$ reception. This may also explain why the early CL (metestrus) is refractory to $\text{PGF}_{2\alpha}$ (Henderson and McNatty, 1977). As the CL ages, gradual dissociation of LH from its receptors occurs. This opens the way for reception of $\text{PGF}_{2\alpha}$ by the membrane. Thus, as the balance shifts toward increasing $\text{PGF}_{2\alpha}$ concentrations over LH concentrations, activation of adenyl cyclase is inhibited within the membrane. This results in declining progesterone secretion and subsequent demise of

the CL.

In opposition to the hypothesis that LH saturation of luteal receptors prevented $\text{PGF}_{2\alpha}$ -induced luteolysis in the early CL, Gonzalez-Mencio et al. (1977) reported the failure of exogenous LH, given to heifers on days 10 to 12 of their cycle, to prevent luteolysis when followed four hours later by 25 mg $\text{PGF}_{2\alpha}$. It may be possible that the loss of binding capacity (Hichens et al., 1974) by days 10 to 12 prevented the exogenous LH from inhibiting the $\text{PGF}_{2\alpha}$ effect.

Other possible proposed mechanisms involve the vasculature of the CL containing ovary. Prostaglandin $\text{F}_{2\alpha}$ contracts all four kinds of smooth muscle and its vasoconstrictive action may induce hypoxia in the ovary, which in turn may lead to luteolysis (Goldberg and Ramwell, 1975). Niswender et al. (1976) noted that declining blood flow to the CL containing ovary or the CL itself are among the first responses during natural luteolysis or after exogenous $\text{PGF}_{2\alpha}$ (as reviewed by Inskeep and Murdoch, 1980). These reviewers cited opposition to decreased blood flow as the mechanism of luteolysis in which total prevention of blood flow to the CL for 45 minutes did not cause CL regression. It has been concluded that reduced blood flow is probably a "consequence" rather than the "cause" of luteolysis (Inskeep and Murdoch, 1980).

McClellan et al. (1977) reported increased lysosomal activity in

regressing luteal cells. This did not occur until after the initial decline in progesterone synthesis. It may be hypothesized that lysosomes are functional in morphological luteolysis but are not involved in initiating functional luteolysis indicated by declining plasma progesterone concentrations.

Types of luteolytic agents. Precocious luteolysis in the bovine can be induced with exogenous oxytocin (Armstrong and Hansel, 1959; Hansel and Wagner, 1960; Ginther et al., 1967) when administered between days 3 and 7 of the cycle. Hansel et al. (1959) reported a 7-day interval in subsequent onset of estrus in heifers receiving oxytocin during the first seven days of their cycle. Fertility to this estrus was comparable to untreated controls but low animal numbers negated significance.

Estrogens have been reported to induce luteolysis when administered to cycling heifers (Wiltbank et al., 1961; Kaltenbach et al., 1964) or cows (Rahlmann and Cupps, 1962) during diestrus. Fertility at the subsequent estrus is low (Wiltbank et al., 1961).

Brunner et al. (1969) studied the luteolytic effects of oxytocin and estrogen by utilizing hysterectomized heifers. They concluded that the luteolytic mechanism of these two compounds involved stimulation of normal uterine mediated luteolysis, which was reviewed in an earlier section.

With the discovery of the luteolytic effects of $\text{PGF}_{2\alpha}$, attention has been turned toward the use of this compound to synchronize bovine females for artificial insemination. A stable tromethamine salt of $\text{PGF}_{2\alpha}$ (THAM) has been developed and is now marketed as Lutalyse[®] (The UpJohn Company). Also, potent $\text{PGF}_{2\alpha}$ analogues (ICI-79939 and ICI-80996, Imperial Chemical Industries) have been synthesized and shown to be effective luteolytic agents in cattle (Tervit *et al.*, 1973; Cooper, 1974; Dobson *et al.*, 1975). Estrumate[®] (ICI-80996, cloprostenol) is marketed in the United Kingdom but is not yet approved for use in the United States.

Extensive research has been carried out in the past ten years to develop effective and efficient treatment systems for $\text{PGF}_{2\alpha}$. Early research determined that $\text{PGF}_{2\alpha}$ was effective only on cattle that are in diestrus of their cycle (days 5 to 16). This includes only about 60% of a randomly cycling herd. To be totally acceptable, systems of treatment were necessary to accommodate animals between days 1 to 4 and 17 to 21 of the cycle.

Small doses of $\text{PGF}_{2\alpha}$ (0.5-6.0 g) administered intrauterinely (IU) were first studied as a method of treatment (Liehr *et al.*, 1972; Rowson *et al.*, 1972; Hafs *et al.*, 1974). The hazard of inducing uterine infections with this method of treatment has prompted the use of other routes of administration (Seguin, 1980). Intramuscular (IM), subcutaneous (SC) and intravenous (IV) injections of 25 to 30 mg

PGF_{2α} or 0.5 mg cloprostenol are effective in inducing luteolysis in cattle (Lauderdale, 1972; Cooper, 1974; Hafs et al., 1974; Stellflug et al., 1975; Lauderdale et al., 1977). Since the IM method is probably the most convenient it has been accepted as the route of administration for producers to use.

Methods of administration. Since PGF_{2α} is only effective on cattle that are in the diestrus, Lauderdale et al. (1974) proposed using rectal palpation of the ovaries to determine reproductive status and treating only those individuals diagnosed to have active CL's. Cows not treated initially are either palpated one week later and treated accordingly or simply injected without palpation. A 30 mg PGF_{2α}-THAM (tromethamine) dose was administered either IM or SC to treated cows. One group of treated cows was inseminated 12 hours after detected estrus for a 7-day period while another was inseminated at 72 and 96 hours post-treatment without regard to estrus. The untreated controls were inseminated 12 hours after estrus during an 18 to 25 day period. Fertility was based on number of animals either responding to PGF_{2α} or observed in estrus. The results showed no difference ($P>.05$) in fertility among treated and untreated cows.

Another method to determine susceptible candidates for PGF_{2α} is heat detection prior to treatment and injecting only those animals which are 5 to 16 days postestrus (Tervit et al., 1973; Macmillan et

al., 1980). Effective synchronization of estrus was reported following this method.

Both of these systems are effective reducing wastage of drug on animals that are not in the proper stage to respond. But, the practicality of applying these methods to range cattle situations is questionable. A more attractive system to beef cattle producers would incorporate a single predetermined timed insemination without the need to detect estrus (appointment breed).

Lambert et al., (1975) first proposed a system whereby a group of beef cows and heifers were detected for estrus and inseminated about 12 hr afterward for a 5-day period. All animals not detected by this time were injected (IM) with 33.5 mg $\text{PGF}_{2\alpha}$ -THAM and inseminated at 12 hr after estrus until 72 hr post-treatment. At this time all unbred cows were inseminated without regard to estrus (appointment bred). The results of this trial indicated as high first service conception rate in the treated group (53%) as in the untreated controls inseminated for a 22 to 30 day period (57%), but, fertility at the 72 hr appointment breeding was low (17%). Daily et al., (1980) also reported low fertility in the appointment bred cows in this system.

Attempts to improve fertility in this system by scheduling the appointment breeding at 80 hr instead of 72 hr post- $\text{PGF}_{2\alpha}$ were reported (Lambert et al., 1976; Donaldson, 1977, Han and Moody, 1979;

Hanks et al., 1980). Conception rates in treated cattle bred to an observed estrus was at least as high as those in untreated controls in all studies. Each of these reports showed a low conception rate in those animals appointment bred without regard to estrus. These reports indicate low fertility in animals bred at an appointment breeding in this system. It may be concluded both the 72 hr and 80 hr appointment breeding are not effective procedures to use after a single $\text{PGF}_{2\alpha}$ injection because extensive wastage of semen results (Donaldson, 1980).

Another system utilizing a single injection of $\text{PGF}_{2\alpha}$ that has been proposed and involves injecting all cows at the beginning of the breeding season and inseminating by estrus for 9 or 10 days (Doornbos and Anderson, 1979; Han and Moody, 1979). Both of these studies reported higher AI pregnancy rates of treated cows than untreated controls inseminated for the same period. This indicated effective synchronization but not all treated animals would respond if there is random distribution of cycling. Therefore wastage of drug occurred in these animals.

Estrous control systems in cattle involving single injections of $\text{PGF}_{2\alpha}$ or its analogues are promising methods for shortening an AI season. Detection of estrus cannot be feasibly eliminated and insemination should be administered only in reference to estrus. Attempts to appointment breed in these systems have failed, probably

due to variation among individuals in the interval from treatment to onset of estrus and ovulation (Johnson, 1978; Refsal and Seguin, 1980).

A practical system using two injections of $\text{PGF}_{2\alpha}$ 10 days apart to synchronize estrus in a group of randomly cycling bovine females was proposed by Inskip (1973) and King and Robertson (1974). This system is based on the theory that the initial injection would regress the CL in all individuals that were between days 5 and 16 of their cycle. These individuals would return to estrus 2 to 4 days later. They would be between days 6 and 8 at the second injection. Those animals in days 17 to 21 at the initial injection would go through a normal estrus and be between days 5 and 9 at the second injection. Those animals between days 0 and 5 at the first injection would be at day 10 through 15 at the second injection. Theoretically, this would place all animals in diestrus to be responsive to the last $\text{PGF}_{2\alpha}$ injection.

Eighty-three percent of 30 cycling Holstein heifers showed estrus 2 to 4 days following treatment in the study by King and Robertson (1974). These results were enlightening, since no pretreatment diagnosis was necessary. Although only 40% of these individuals conceived to inseminations at observed estrus and 12 hr later, this was not different from 54% of control heifers that conceived to similar inseminations.

Preliminary results reported by Cooper (1974) showed similar

success in 130 dairy heifers receiving two 0.5 mg cloprostenol injections 10 to 12 days apart. Eighty-nine of these animals were inseminated 12 hr after detected estrus following treatment. Another 30 treated heifers were inseminated twice at 72 and 96 hr after the second injection without regard for estrus. Conception rates based on rectal palpation eight weeks after breeding were identical in both treated and untreated groups. In addition this author reported a detailed study on another 45 heifers receiving two injections of 0.5 mg cloprostenol 11 days apart. Of 43 heifers showing estrus after treatment, 39 were detected between 48 and 72 hr after the second injection; the other four were observed in estrus between 72 and 96 hr post-treatment. Ovulation occurred in 4 heifers between 48 and 72 hr, 34 heifers between 72 and 96 hr and 5 heifers between 96 and 120 hr post-treatment.

Due to the shorter interval of estrus following this treatment the possibility of using an appointment breeding seemed more promising. Hafs *et al.*, (1975a) used two IM injections of PGF_{2α} 12 days apart on dairy heifers and suckled beef cows to synchronize estrus. Treated heifers were inseminated twice at 70 hr and 88 hr post treatment with semen from the same bull. Treated cows were inseminated once with semen from one breed of bull at 70 hr post-treatment and again at 88 hr post-treatment with semen from another breed of bull. Using calving data to determine results, they reported 54% conception in

heifers bred at 70 and 88 hr post-PGF_{2α} compared to 55% conception in untreated heifers; these were inseminated after detected estrus for a three-week period. Forty-one percent of the treated cows conceived to the timed inseminations compared to 44% of the untreated cows conceiving to insemination after an observed estrus for a 25-day period. Highest fertility in the treated animals was among individuals detected in estrus 3 to 5 days after treatment. Sixty-eight percent of the treated heifers and 62% of the treated cows showed estrus during this period. More treated cows conceived to the 70-hr insemination than to the 88-hr insemination although the difference was not substantiated. The authors conjectured that a single insemination at 80-hr post-treatment could produce satisfactory results.

A large field trial was conducted on 960 heifers and 392 beef cows to test the feasibility of an 80 hr appointment breeding (Hafs et al., 1975b). Treated animals received two injections of either 0.5 mg cloprostenol or 30 mg PGF_{2α}-THAM 10 to 12 days apart. One group of treated animals was inseminated twice at 70 and 88 hr after treatment. The other treated group was inseminated once at 80 hr post-PGF_{2α}. Untreated controls were inseminated following observed estrus. In the controls bred after detected estrus, 51% of the heifers and 59% of the cows were diagnosed pregnant based on either rectal palpation or nonreturn rate. Among treated animals 63% of the heifers and 58% of

the cows inseminated twice were diagnosed pregnant while 62% of the heifers and 57% of the cows inseminated once were pregnant. The authors reported no difference in fertility after $\text{PGF}_{2\alpha}$ -THAM or cloprostenol treatment. They concluded fertility after $\text{PGF}_{2\alpha}$ treatment was equivalent to controls and fertility from one insemination (80 hr) was equal to that from two inseminations (70 and 88 hr) after prostaglandin.

Hafs et al., (1978) reported similar fertility results in heifers and beef cows receiving two $\text{PGF}_{2\alpha}$ injections 11 days apart and either inseminated twice at 70 and 88 hr post-treatment or once at 80 hr post treatment. Also, they reported that only 15% more semen was used on the treated cows inseminated once (80 hr) than that used on the untreated controls. The two insemination system required 107% more semen than the untreated controls.

Another predetermined (appointment) breeding time of 72 hr post- $\text{PGF}_{2\alpha}$ was studied. Cooper et al. (1976) reported lower conception in cows and heifers inseminated once at 72 hr after two injections of cloprostenol 11 days apart than that in treated animals inseminated twice at 72 and 96 hr post- $\text{PGF}_{2\alpha}$ or controls bred by natural service for 21 days. Over 3,000 animals were used in this study. Similar results following this system were reported by Schultz et al., (1977).

Moody and Lauderdale (1977) compared insemination after two $\text{PGF}_{2\alpha}$ injections in beef cows either at 80 hr post-treatment or after

detected estrus from day 2 to 5 post treatment. They reported significantly lower first service conception rates in the 80-hr appointment bred group than in the treated cows or untreated controls inseminated after detected estrus. The total pregnancy rate (number pregnant $\div$ total in group) for the appointment bred group was not different from that in the treated group inseminated only after detected estrus. Both treated groups had a significantly higher total pregnancy rate by day 5 of the breeding season than the untreated controls.

Results of these trials using two injections of PGF_{2 α} 10 to 12 days apart to synchronize estrus in cattle indicate that this may be a feasible system to utilize AI without heat detection. The 80 hr appointment breeding is probably the better timed insemination. Many factors have been pointed out in the literature that may help to contribute to the success of this breeding system. The variability in the onset of estrus and ovulation following this treatment may be a problem in lactating dairy cows (Macmillan, 1978; Roche and Prendiville, 1979); for heifers this does not appear to be a problem (Johnson, 1978; Refsal and Sequin, 1980) but is marginal in beef cows (Hafs et al., 1975a). But, it has been reported that this synchronization system is not successful in Brahman cattle (Hardin et al., 1980). Seasonal variations of onset of estrus following PGF_{2 α} in heifers were reported by Britt et al. (1978). One major benefit of

this system was reported by Esselmont et al. (1977). These authors evaluated the reproductive efficiency of animals receiving this treatment and found that the intervals from the beginning of the breeding season to first service and conception were significantly reduced by 13.6 and 12.5 days, respectively, compared to untreated controls.

Due to the variation in onset of estrus after $\text{PGF}_{2\alpha}$ treatment in cattle, studies were conducted to increase the precision of synchrony by incorporating estrogen into the treatment regimen. It is hypothesized that this would induce a more synchronized estrus and ovulation. Injections of E_2 48 hr after either a double $\text{PGF}_{2\alpha}$ injection system or intra-uterine infusions of $\text{PGF}_{2\alpha}$ in beef females were effective in increasing the precision of synchrony. Fertility after treatment was comparable to that in untreated controls and $\text{PGF}_{2\alpha}$ -alone treated females (Inskeep et al., 1975; Welch et al., 1975; Peters et al., 1977). Practical application of this system may not be acceptable to beef producers due to the added cost of treatment and the extra handling of animals.

The use of GnRH injections after $\text{PGF}_{2\alpha}$ treatment to more precisely synchronize the LH peak and subsequent ovulation has been studied. It was hypothesized that this may improve fertility in a group of cows bred at an appointment breeding. Failure to accomplish this was reported by Tobey and Hansel (1975), Kinkie (1976) and

Burfening et al. (1978) when 100 ug GnRH was injected 60 hr after PGF_{2α} and insemination at 72 hr post-PGF_{2α}. GnRH is reported to suppress behavioral estrus in cattle when administered after PGF_{2α} (Thatcher and Chenault, 1976; Rodriquez et al., 1975), although this was not evident in a study by Britt et al. (1975) when GnRH was administered 11 days prior to the first PGF_{2α} injection.

Use of Progestagen and Luteolytic Agent Combinations.

Mechanism of Control. Long term use of progesterone or progestagens (i.e., 16 to 21 days) results in acceptable synchronization of estrus in bovine females but fertility is lower than normal at the estrus after treatment. However, acceptable fertility in bovine females is accomplished when progestagen treatment is shortened to 9 to 12 days, but effective synchronization is lowered due to failure of luteolysis to occur in some treated animals. It has been hypothesized that a luteolytic agent incorporated at the initiation of a 9-day progestagen treatment would insure luteolysis and would result in a more acceptable estrous synchronization and fertility rate (Lamming et al., 1979).

Methods of administration. Successful estrous synchronization and acceptable fertility following 9 to 12 day progestagen treatment with injections of E₂ administered when treatment is initiated in bovine females were reported using sponge pessaries (Sreenan, 1975;

Sreenan and Mulvehill, 1975) and PRID (Roche et al., 1976; Drew et al., 1978). Variable success was reported when E₂ injections were administered at initiation of a 9-day subcutaneous-implant treatment regimen (Anderson et al., 1969; Wiltbank et al., 1971; Burrell et al., 1972; Whitman et al., 1972). Other research in this method showed that by increasing the level of progestagen in the implant (Woody and Abenes, 1975), placing the progestagen in the wall and the lumen of the implant (Wideman et al., 1969) and (or) administering an injection of progestagen, along with the estrogen at the time the implant was inserted (Wishart and Young, 1974; Wishart et al., 1977) resulted in more acceptable synchrony and fertility. It is hypothesized that this was due to an antiluteotropic effect produced by the higher initial level of progestagen on CL that were just developing at the initiation of treatment (Lamming et al., 1979). This led to the development of a synchronization system known as Synchro-Mate-B[®] (SMB, G.D. Searle Co.). This system consists of a silastic implant containing 6 mg norgestomet (SC-21009) placed subcutaneously in the ear for 9 days and a single injection of 6 mg E₂ and 3 mg norgestomet administered at time of implant insertion. Successful synchronization of estrus and fertility at a timed insemination 48 to 54 hr after implant removal in heifers receiving this system was reported by Wiltbank and Spitzer (1978). The SMB treatment was not as successful in suckled beef cows (Goodell et al., 1976), but some improvement was noted after

incorporating GnRH injections prior to insemination (Zaied et al., 1976) or calf removal for 24 to 48 hr (Shang) prior to timed inseminations (48 to 54 hr post-treatment) (Mares et al., 1977; Kaltenbach and Dunn, 1979; Kiser et al., 1979; Peterson et al., 1979). One benefit of progestagen-luteolysin combination systems is that they may induce cycling activity in anestrous cows (Drew et al., 1978; Mares et al., 1979) and prepubertal heifers (Gonzalez-Padilla et al., 1975).

Combinations of progestagens and $\text{PGF}_{2\alpha}$ have been studied in which $\text{PGF}_{2\alpha}$ was administered at or near the end of a 5 to 8 day progestagen treatment. Fertility of beef and dairy females receiving this treatment was reported to be satisfactory (Wishart, 1974; Roche, 1976b; Stauffer et al., 1976; Chupin et al., 1977). Moody et al. (1980) were unable to show evidence that injections of P_{14} either 24 or 5 days prior to a single $\text{PGF}_{2\alpha}$ injection effectively improved reproductive performance in beef heifers. The major problem was a low cycling rate (60%) in these animals. This was determined by the rate of detection of estrus in untreated controls for a 10-day period. These results further suggest that this system, like all other systems of synchronization discussed in this review, is most acceptable to producers when it is used on actively cycling bovine females.

STATEMENT OF PROBLEM

Prostaglandin $F_{2\alpha}$ is the only synchronization agent that is approved by the Food Drug Administration for use by United States beef and dairy producers. Artificial insemination at 80 hr (appointment breeding) after two injections of $PGF_{2\alpha}$ 10 to 12 days apart is probably the most inviting breeding system because it negates the need for detecting estrus. The efficiency of this system has not been satisfactory to producers because of lower than expected production of AI calves, especially in range beef operations. The objectives of these studies were: 1) to determine if estrus can be synchronized in suckled beef cows (at least 50 days post-partum) with two injections of $PGF_{2\alpha}$ 11 days apart; 2) to determine if pregnancy rate from artificial insemination at 12 hr after detected estrus up to 80 hr after treatment then the residual (i.e., not detected by 80 hr post-treatment) bred at 80 hr is different from that when artificial insemination occurs only at 80 hr after this double injection system; 3) to determine if pregnancy rate from artificial insemination is influenced by time of estrus following treatment and either bred at 12 hr after estrus or at 80 hr (appointment bred); 4) to determine the distribution of estrus in suckled beef cows after a single $PGF_{2\alpha}$ injection system; 5) to compare artificial insemination pregnancy rates and total pregnancy rates in a 50 day breeding season in suckled beef cows receiving either heat detection and insemination 12 hr afterward for 4.5 days then all animals not detected by that time

injected with $\text{PGF}_{2\alpha}$ and inseminated after detected estrus for four more days or two injections of $\text{PGF}_{2\alpha}$ 11 days apart and inseminated only at 80 hr after treatment; and 6) to compare calving rates at various stages of the season in beef cows bred after either a single $\text{PGF}_{2\alpha}$ injection system or a double $\text{PGF}_{2\alpha}$ injection system with an 11 day interval between injections.

Materials and Methods

Animals. Three herds of suckled beef cows located in the intermountain region of Montana were used in these studies and included: Herd I) 299 Angus and Angus x Hereford cows, 3 to 5 years old, at the Dana Ranch Company, Cascade, Montana; Herd II) 138 Angus and Angus x Hereford cows, 2 to 10 years old, at the Red Bluff Experiment Station, Norris, Montana; and Herd III) 219 mostly Angus, Hereford and Hereford cross cows, 3 and 4 years old, at the Montana State Prison Ranch, Deer Lodge, Montana. All cows were at least 50 days post-partum when treatments were initiated and were nursing calves.

Trials and Treatments.

Trial 1. Cows within a herd were assigned at random to one of three treatment groups which included: 1) controls which were artificially inseminated (AI) 12 hr after detected estrus; 2) cows receiving two injections of Lutalyse[®] (25 mg $\text{PGF}_{2\alpha}$ free acid

equivalent) 11 days apart followed by insemination 12 hr after detected estrus until 80 hr post-treatment at which time all cows not yet detected were inseminated (LL-AI-E-80); and 3) cows receiving the same PGF_{2α} treatment as in treatment 2 but inseminated only at 80 hr post-treatment (LL-AI-80) (fig.1). This trial involved all the experimental animals from all three herds.

Trial 2. This trial involved only the experimental animals in Herds II and III that were assigned to the control and LL-AI-80 groups in trial 1. The control animals in these herds were detected for estrus and inseminated 12 hr afterward for 4.5 days and all members not detected up to that time received a single injection of Lutalyse^R and detection of estrus and insemination continued for 4 more days (AI-L-AI-E). The LL-AI-80 group in trial 2 consisted of the same LL-AI-80 cows from these two herds in trial 1 (fig. 2).

Detection of estrus and breeding.

All cows within a herd were retained in the same foothill pasture during the AI season. Observations for estrus began immediately after the second PGF_{2α} injection for all groups and were executed by trained technicians at least twice daily for periods of one hour or more during the early morning and evening hours. Estrus was identified as standing to be mounted by herdmates. Estrus was recorded for members of all groups in each herd during their respective AI season. Since

the LL-AI-E-80 and LL-AI-80 groups in trial 1 received the same PGF_{2α} treatment their estrus data were combined to derive a distribution of onset of estrus after this treatment. A distribution of onset of estrus in the control group in trial 1 was tabulated for a four-day period. A distribution of estrus in the AI-L-AI-E group in trial 2 was tabulated for those animals receiving PGF_{2α}.

The same trained technicians performed the artificial inseminations in all three herds. All cows that were bred in regard to estrus were artificially inseminated 12 hr after they were detected in estrus. Cows in the LL-AI-E-80 and LL-AI-80 groups that were detected in estrus after 96 hr post-PGF_{2α} (16 hr after 80 hr breeding) were reinseminated 12 hr after detected estrus with semen from a bull of a breed different from that used at the 80-hr breeding to provide a genetic marker to determine sire of calf. In Herd I, Black Angus semen was used in the control cows and in the PGF_{2α}-treated cows through the 80 hr breeding. Polled Hereford semen was used for the second inseminations in the cows that were treated. The AI season was 6 days for this herd and Black Angus clean-up bulls followed. In Herd II, first inseminations were with Tarentaise semen in all groups for both trials. Second inseminations were with Polled Hereford semen in Angus cows and Shorthorn semen in the Hereford x Angus cows. The AI season was 8.5 days in this herd and Black Angus clean-up bulls followed. In Herd III, first inseminations in the LL-AI-E-80 and LL-

AI-80 groups were with Polled Hereford semen. Second inseminations in these groups were with Black Angus or Longhorn semen. Control cows in trial 1 (AI-L-AI-E in trial 2) were inseminated with either Longhorn or Polled Hereford semen. The AI season was 8.5 days and Brahman cross, Red Angus, Black Angus and Hereford clean-up bulls followed. Clean-up bulls were introduced about 12 hr after the last AI in all herds. These herds were then moved to mountain summer pastures and bulls remained with the cows until the end of a 50-day breeding season (AI plus natural service).

Statistical Analyses.

Onset of estrus, breeding and calving records supplied the data for these trials.

Trial 1. Cumulative AI pregnancy rates (number of animals pregnant $\div$ number in group) for the first four days of the breeding season were used to compare systems. Calving and breeding records were used to determine the sire of the calf (AI versus clean-up) and the genetic markers within a herd were the main criteria. Gestation lengths of 286 days for Hereford and Hereford cross, 281 days for Angus and 283 days for other breeds were used when genetic markers did not satisfactorily determine the sire. Other criteria such as birth weight and sex of calf along with observed heats and an average 21 day estrous cycle for cows were also incorporated.

Initially, individual data analysis for each herd was performed. Contingency Chi-square (Steel and Torrie, 1976) was used to analyse differences among treatments and to combine onset of estrus data among herds. A log-linear model for attribute data (Fienberg, 1977) was used to test for herd x treatment interaction to combine the pregnancy rate data.

Trial 2. First service AI pregnancy rates during the 8.5 day AI season were compared between systems. Cumulative calving rates by 17, 38 and 60 days of calving were computed and compared. Calving intervals began on the day the first calf was born. Allowance for variation among individuals of seven days gestation was incorporated to approximate calving from pregnancy in the first 10, 31 and >50 days of breeding. These were determined through breeding and calving records. Contingency Chi-square was used for statistical analyses of these data and a level less than 5% was considered significant.

Results

Trial 1. The number of cows in both the control and combined PGF_{2α}-treated groups for the three herds in this study are depicted in table 1. Percentage distributions of estrus after four days of detection in the combined herds are shown in figure 3. Thrity-four percent of the PGF_{2α}-treated cows and 17% of the control cows ($P < .05$) were observed in estrus during this period. Therefore, this double

injection treatment was effective in synchronizing estrus.

Behavioral estrus occurred in the double injected cows through at least day 6 post-treatment. The combined herds distribution of estrus in the $\text{PGF}_{2\alpha}$ -treated cows (fig. 4) demonstrates that there is variation of at least 5 days (days 2-6) in the interval from this treatment to onset of estrus in beef cows. Two hundred-eighteen (50%) of these animals were detected during this 5-day period. The majority (58%) of these were detected on day 3 or 4 following treatment. Another 32% were detected on day 5 or 6, while 10% were observed on day 2. Observations for estrus continued for 2.5 more days in Herds II and III. Only 3 (1.3%) of these animals were detected during this period and these were all in Herd III and were detected on day 7.

Calving records for 53 and 29 of the experimental cows in Herds I and III, respectively, were unavailable after the calving season. These losses were attributed mostly to misidentification of cows

TABLE 1. COW DISTRIBUTION BY HERD AND GROUP IN THREE HERDS OF SUCKLED BEEF COWS RECEIVING TWO INJECTIONS OF $\text{PGF}_{2\alpha}$ 11 DAYS APART

Herd	Control	Treated	Total
Herd I	103	196	299
Herd II	47	91	138
Herd III	74	145	219
Total	224	432	656

either at calving or during sorting of experimental members from their herdmates prior to calving. These individuals were randomly distributed among treatment groups and were deleted from the fertility data.

Cumulative pregnancy rates from AI during the first four days of the breeding season are shown in table 2. Cumulative pregnancy rate equals the number of animals pregnant divided by the number of animals in the group. In the analysis of all three herds and the combined herds there was a higher ($P < .05$) 4-day pregnancy rate in the treated groups than in the controls. Results from Herds I and II indicated a trend for a higher 4-day pregnancy rate in the LL-AI-E-80 group than in the LL-AI-80 group although the differences were not significant ($P > .05$). The reverse trend was noted in Herd III. Herd x treatment interaction analysis approached significance ($P < .09$). This reveals that there was a tendency for herds to respond differently to these breeding management systems, but this difference was not pronounced. Calf production from artificial insemination was not different ($P > .05$) between these two breeding systems in the combined herds.

Of those cows observed in estrus during the first four days of detection, the pregnancy rates (number of cows pregnant $\div$ number of cows observed in estrus) did not differ ($P > .05$). Differences among groups were noted in pregnancy rate within those 12-hr intervals of detection in which at least one individual from all groups was

observed in estrus. These intervals included 36-48, 48-60, 60-72 and 84-96 hr after PGF_{2α} treatment. Within the LL-AI-80 group the pregnancy rate of those animals detected in estrus remained constant ($P>.05$) among the 12-hr intervals in which estrus was detected.

The reproductive performance during the 6-day detection period of the remaining treated cows is shown in table 4. These animals included those not detected in estrus during this period and those detected on day 5 or 6. None of the treated animals in estrus on day 5 or 6 were pregnant from the appointment breeding. All of these cows were repeat-inseminated at 12 hr after being detected and 71% of 28 LL-AI-E-80 cows and 77% of 35 LL-AI-80 cows were pregnant to these inseminations. These pregnancy rates did not differ ($P>.05$) either between treatment groups or from untreated controls that were inseminated. Eighty-seven of the LL-AI-E-80 cows and 97 LL-AI-80 cows were not observed in estrus during the 6-day detection period and of these, 37 and 39%, respectively, ($P>.05$) were pregnant from inseminations at the appointment breeding.

Trial 2. Thirty-nine (83%) and 59 (88%) ($P>.05$) of the cows in the AI-L-AI-E group in Herds II and III, respectively, were not observed in estrus during the first 4.5 days of detection and received PGF_{2α} (table 5). Of those receiving PGF_{2α}, 29 (74%) and 40 (68%) ($P>.05$) in Herds II and III, respectively, were detected during

the following 4 days. In the combined herds 58 (59%) of the injected cows were observed in estrus between 36 and 96 hr after $\text{PGF}_{2\alpha}$. This represents the peak period of estrus in this group and demonstrates that this system is effective in synchronizing estrus. This agrees with Hafs *et al.*, (1975a) who reported a peak response between 48 and 120 hr post- $\text{PGF}_{2\alpha}$ in suckled beef cows after a single injection of $\text{PGF}_{2\alpha}$.

A comparison of the reproductive performance of these cows in 8.5 days of AI to that of their herdmates in the LL-AI-80 breeding system is shown in table 5. The first AI pregnancy rate (number pregnant to first AI $\div$ number receiving first AI) was higher ($P < .05$) in the AI-L-AI-E group than in the LL-AI-80 group in Herd III and the combined herds. The same trend was noted in Herd II but the difference was not significant ($P > .05$). Total AI pregnancy rate (number pregnant to first AI $\div$ number in group) was not different ($P > .05$) between groups in either herd or the combined herds.

Discussion

The variation in the interval from treatment to onset of estrus found in trial 1 concurs with results reported by Hafs *et al.*, (1975a). Since $\text{PGF}_{2\alpha}$ does not alter the average time (24-32 hr) from onset of estrus to ovulation (Louis *et al.*, 1974), it may be hypothesized that the lower than satisfactory production from the LL-

AI-80 system is due to inseminating cows too early or too late in relation to ovulation. Those cows showing estrus more than 20 hr prior to the appointment breeding would not be expected to conceive (as reviewed by Lauderdale, 1974). These data (table 3) show that inseminating as late as 32 hr or more after detected estrus (cows detected during the 36-48 hr post-treatment interval) still resulted in pregnancy from the appointment breeding. Also, those animals inseminated between 20 and 32 hr after estrus were pregnant at the same rate as those inseminated 12 hr after observed estrus. Conception rates to inseminations 24 hr after observed estrus have been reported to equal those to inseminations 12 hr after estrus in beef heifers (Vincent and Turner, 1972) and dairy cows (Gwasdauskas and Lineweaver, 1981). It may be suggested that fertility to inseminations at 80 hr after this $\text{PGF}_{2\alpha}$ treatment is not affected by time of onset of estrus prior to this appointment breeding.

Four of seven treated cows that were observed in estrus between 4 and 16 hr after the appointment breeding were pregnant to that insemination. This pregnancy rate was not different from that either in cows which were in estrus prior to the appointment breeding at which they were bred or in cows bred by estrus. Similar results in progestogen synchronized cows were reported by Carrick and Shelton (1967).

Thirty-eight percent of the treated cows (70 of 184) which were

not detected in estrus during the detection period were pregnant from the appointment breeding. These animals may have either failed to be detected or ovulated without behavioral estrus (Donaldson, 1977). Most of the detection failures, if they did occur, may have resulted due to mass handling of the herds during the appointment breeding. This could have prevented the estrus animals from displaying behavioral estrus. Also, the attention of the technicians at this time was toward inseminating and away from detecting. But, the stress of handling probably would not have prevented physiological estrus (Wagnon, et al., 1972; Mawhinney and Roche, 1980). Conversely, Hardin et al., (1980) cited evidence that timed inseminations could suppress behavioral estrus by stimulating a premature release of preovulatory LH resulting in an inhibition of follicular estrogen secretion necessary for this behavior to occur. Lauderdale et al., (1974) and Burfening et al., (1978) observed that some cows become pregnant without exhibiting estrus when bred by appointment after PGF_{2α}.

If the AI pregnancy rate of these undetected animals is similar to that of the untreated controls (69%), then approximately 100 of the undetected treated animals ovulated without being detected in estrus. Furthermore, if all cows detected during the 6-day period did so in response to the treatment (99 LL-AI-I-80 plus 92 LL-AI-80, 191 total) then the two injection PGF_{2α} treatment was effective on 78% (291 of 375) of the treated cows.

The difference in first AI pregnancy rate in trial 2 indicates that the efficiency of the AI-L-AI-E system is better than the LL-AI-80 system in terms of the amount of semen needed to acquire the same number of AI calves (total AI pregnancy rate, $P > .05$). However, 8.5 days of heat detection were necessary to do this. Heat detection was not used in the LL-AI-80 system. The amount of drug used in the LL-AI-80 system was 122% more than that used in the AI-L-AI-E system. The net result is an equal number of AI calves from either system, but the trade-offs are more drug and semen for less time and labor for detecting estrus.

One possible advantage of the two injection system is illustrated in table 7. Significantly more calves were born during the first 38 days of calving in the LL-AI-80 system than in the AI-L-AI-E system in Herd III and the combine herds. A similar trend, although not different was noted in Herd II. This added grouping effect at calving adds merit to the LL-AI-80 system.

Jackson *et al.*, (1979) reviewed and supported evidence that estrus and ovulation after a single $\text{PGF}_{2\alpha}$ injection in diestrus cows varied over a wider range than estrus and ovulation after two injections 11 days apart. Thus, the closer grouping effect of calving in the LL-AI-80 system than in the AI-L-AI-E system may have resulted from more animals having at least two opportunities to become pregnant and calve within the first 38 days in the double injection

system. Those individuals that responded later in the single injection system may not have had another opportunity to become pregnant and calve during this interval if their cycle length was at the extreme end of the average 17 to 24 day interval.

The reproductive efficiency of treated groups in either of these studies was not high (approximately 50% total AI pregnancy rate). Some improvements in efficiency may result from more critically selecting candidates for these breeding management systems. Wiltbank (1970) reviewed evidence that indicate maximal conception rates are obtained when beef cows are at least 60 days post-partum. The animals used in these studies were 50 or more days postpartum.

Some modification of either system in trial 2 may yield more satisfactory results. Donaldson (1980) reported that the efficiency of an AI-L-AI-E system in which cows were detected and inseminated for 5 days prior to the residual PGF_{2α} treatment and inseminated for a 10 day total period was equal to the efficiency of inseminating untreated controls for 21 days. In this study a 4.5 day pretreatment period and an 8.5 day total AI period were used.

More AI calves may be acquired in the LL-AI-80 system by heat detecting and repeat inseminating treated cows between 96 and 144 hr after treatment. The failure of animals showing estrus during this period to become pregnant to the appointment breeding is demonstrated in trial 1 (table 4). The fertility of these animals to the repeat

inseminations is at least as good as that in untreated controls inseminated after detected estrus. This procedure would require 15 to 20% more semen (fig. 4). If clean-up bulls are used immediately following the appointment breeding they should not be introduced until at least 16 hr later. Cows that show estrus up to that time do conceive to the appointment breeding.

Conclusions

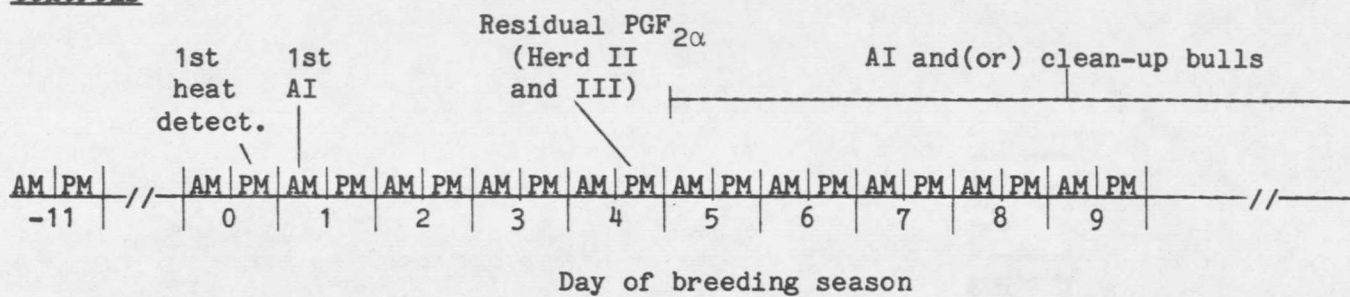
Two injections of 25 mg $\text{PGF}_{2\alpha}$ 11 days apart does synchronize estrus in suckled beef cows which are at least 50 days post partum. There is a variation in the interval from treatment to onset of estrus of at least 5 days (days 2 through 6 post-treatment). The pregnancy rate from artificial insemination administered either 12 hr after detected estrus up to 80 hr post-treatment then all animals not yet inseminated are inseminated at this time or only at 80 hr post-treatment is not different following this double injection treatment. This is because pregnancy rate from an 80 hr appointment breeding in suckled beef cows is not influenced by time of onset of estrus that occurs before 96 hr post-treatment. Therefore, an 80 hr appointment breeding should be used after this double injection $\text{PGF}_{2\alpha}$ treatment in suckled beef cows and heat detection up to 96 hr post-treatment is not required; also, some cows become pregnant to this insemination without displaying estrus through a 6-day post-treatment period. Those

animals that show estrus after 96 hr post-treatment do not become pregnant to an 80 hr breeding. If calves from artificial insemination are desired from these animals it is necessary to reinseminate these cows after being detected in estrus. This reinsemination period would last only about 48 hr and approximately 20% more semen would be required. A system involving detecting estrus for 4.5 days then injecting all cows not yet detected and detecting estrus for 4 more days shows that estrus in suckled beef cows (at least 50 days postpartum) is synchronized with one injection of 25 mg $\text{PGF}_{2\alpha}$. There is no difference in the number of calves produced from artificial insemination when beef cows are either inseminated 12 hr after detected estrus in this single injection system or inseminated without regard to estrus at 80 hr after two injections of $\text{PGF}_{2\alpha}$ administered 11 days apart. The choice between which of these two breeding management systems to use on suckled beef cows should be based on the amount of time, pasture and labor available for detecting estrus as opposed the extra cost for more drug and semen necessary to alleviate these requirements.

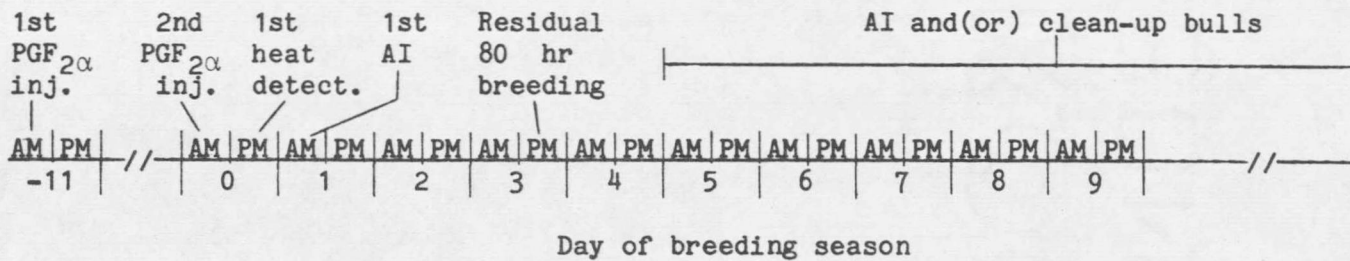
One possible advantage of the double injection $\text{PGF}_{2\alpha}$ system is that more calves are born in the first 38 days of calving following this treatment than following the single injection treatment. This adds merit to the LL-AI-80 system because more calves in a group would be similar in age.

APPENDIX

Controls



LL-AI-E-80



LL-AI-80

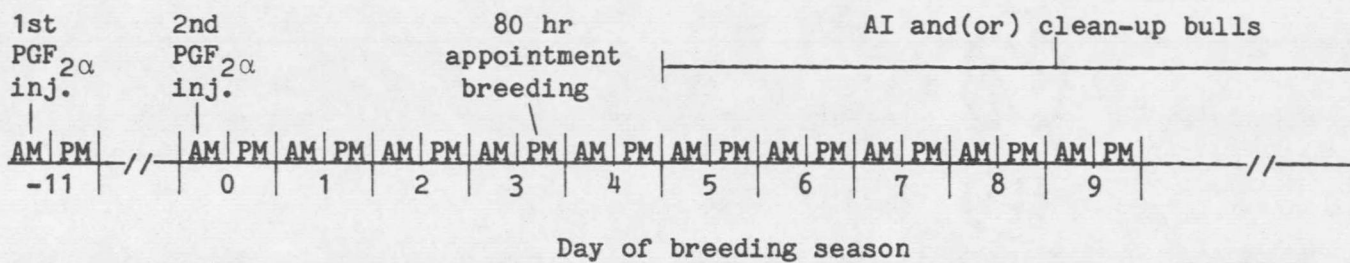
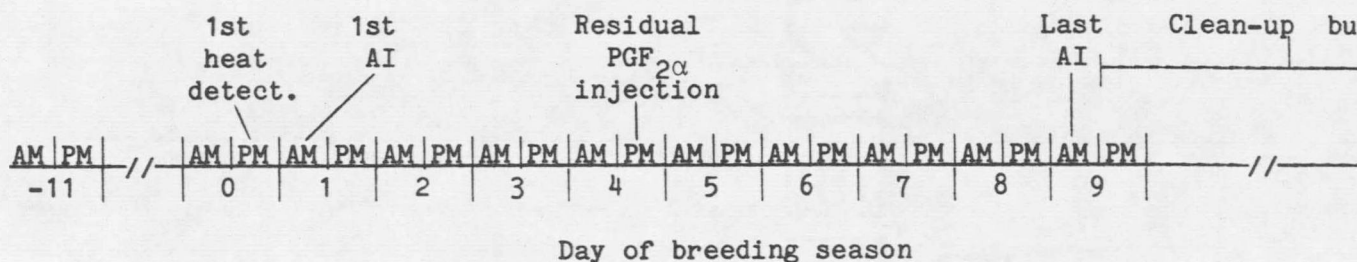


Figure 1. Design of breeding management systems in trial 1.

AI-L-AI-E



LL-AI-80

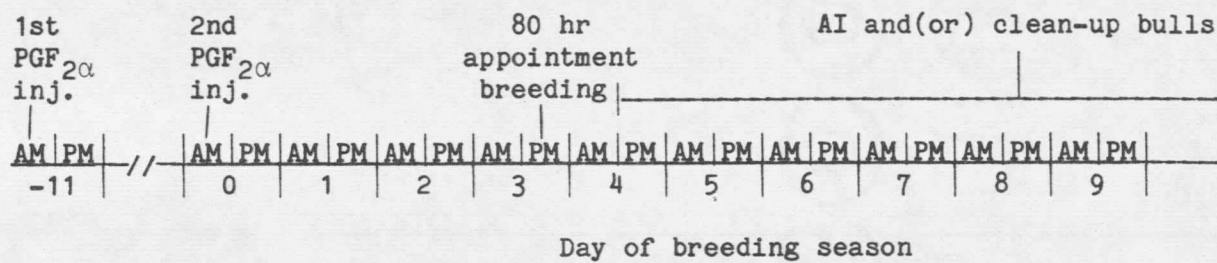


Figure 2. Design of breeding management systems in trial 2.

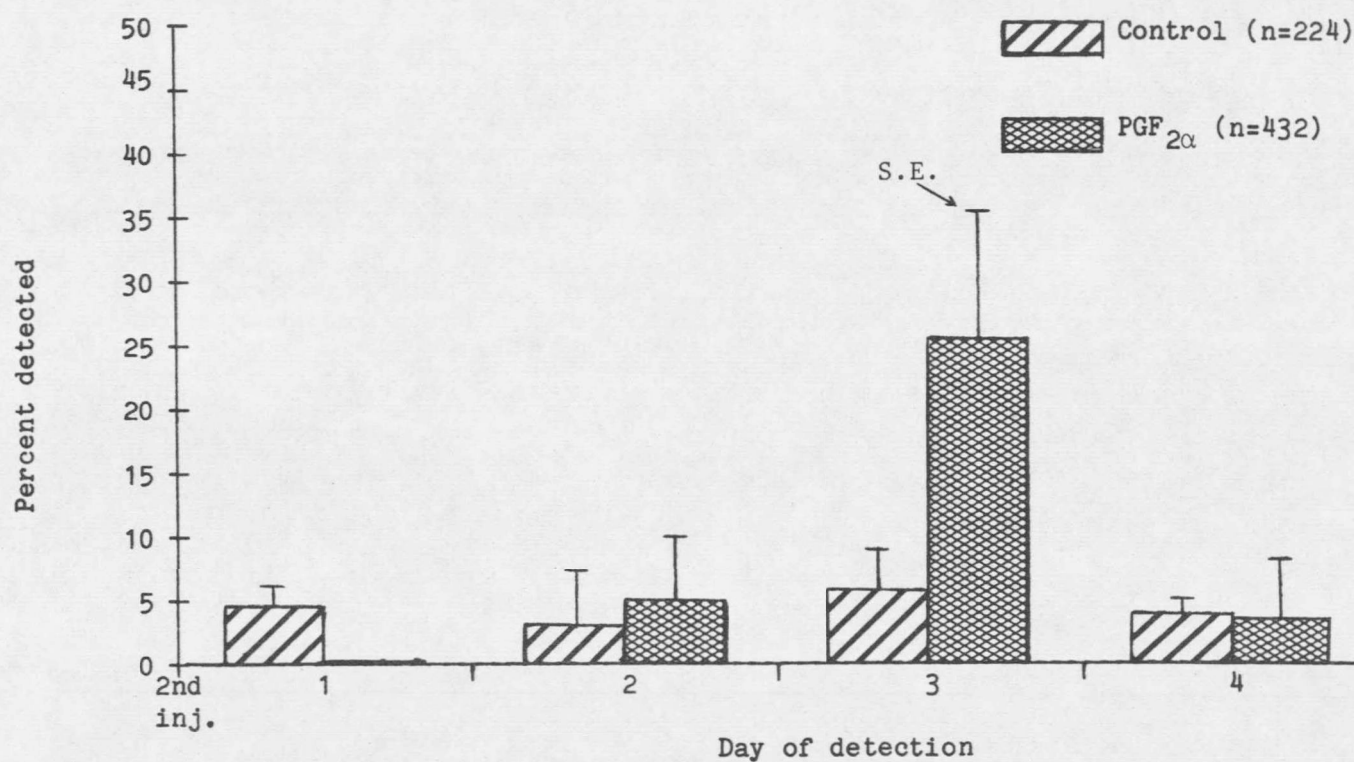


Figure 3. Percent distribution (means $\pm$ S.E.) of estrus in controls and cows receiving two injections of PGF_{2α} 11 days apart in three herds of suckled beef cows.

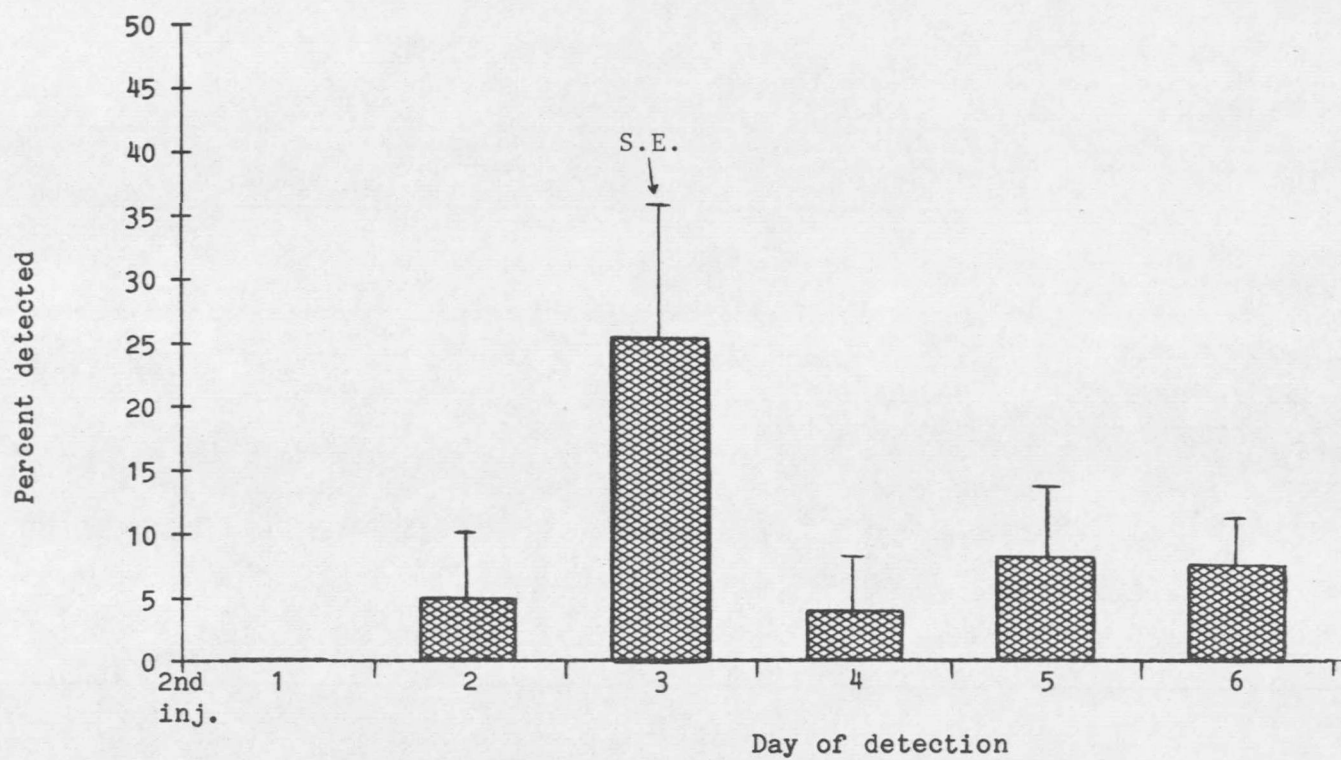


Figure 4. Percent distribution (means $\pm$ S.E.) of estrus in three herds of suckled beef cows receiving two injections of $\text{PGF}_{2\alpha}$ (25 mg) 11 days apart ($n=432$).

TABLE 2. CUMULATIVE AI PREGNANCY RATES BY DAY FOUR OF BREEDING SEASON FOLLOWING UNTREATED CONTROL, LL-AI-E-80 AND LL-AI-80^a

	<u>Breeding Management Systems^{aa}</u>		
	Control	LL-AI-E-80	LL-AI-80
Herd I			
Number of animals	87	79	80
Number observed in estrus	20	23	--
Number pregnant	11	32	22
Cumulative AI pregnancy rate	13% ^a	41% ^b	28% ^b
Herd II			
Number of animals	47	46	45
Number observed in estrus	7	25	--
Number pregnant	6	30	22
Cumulative AI pregnancy rate	13% ^a	65% ^b	49% ^b
Herd III			
Number of animals	67	61	64
Number observed in estrus	8	24	--
Number pregnant	7	22	29
Cumulative AI pregnancy rate	10% ^a	36% ^b	45% ^b
Combined herds			
Number of animals	210	186	189
Number observed in estrus	35	71	--
Number pregnant	24	84	73
Cumulative AI pregnancy rate	12% ^a	45% ^b	39% ^b

^aCumulative AI pregnancy rate equals number of animals pregnant ÷ number of animals in group.

^{aa}Herd x treatment interaction (P<.09).

a,b Means with different superscripts within rows are significantly different (P<.05).

TABLE 3. PREGNANCY RATES OF COWS DETECTED IN ESTRUS DURING THE FIRST FOUR DAYS OF DETECTION FOLLOWING UNTREATED CONTROL, LL-AI-E-80 AND LL-AI-80¹

Interval after PGF _{2α} (hr)	Breeding Management Systems					
	Control		LL-AI-E-80		LL-AI-80	
	Detected	Pregnant	Detected	Pregnant	Detected	Pregnant
0 - 12	3	1	0	0	0	0
12 - 24	6	4	0	0	0	0
24 - 36	5	3	1	1	0	0
36 - 48 ²	2	2	13	7	6	6
48 - 60 ²	6	3	33	26	36	36
60 - 72 ²	5	4	19	15	12	12
72 - 84	2	2	1	1	0	0
84 - 96 ²	6	5	4	2	3	3
Total	35	24	71	52	57	57
Total pregnancy rate ²	69%		73%		61%	

¹Pregnancy rate equals number of cows pregnant - number of cows detected.

²Pregnancy rates among systems were not significantly different (P>.05).

³Pregnancy rates among intervals were not significantly different (P>.05).

TABLE 4. PREGNANCY RATES OF COWS EITHER DETECTED IN ESTRUS ON DAYS FIVE OR SIX OR DETECTED DURING THE FIRST SIX DAYS OF THE DETECTION PERIOD FOLLOWING LL-AI-E-80 AND LL-AI-80¹

	Breeding Management Systems					
	LL-AI-E-80			LL-AI-80		
	Number of cows	Number pregnant to 80 hr breeding	Number pregnant to repeat breeding	Number of cows	Number pregnant to 80 hr breeding	Num preg to rep breed
Estrus (day 5 or 6)						
Herd I	11	0	8	13	0	11
Herd II	8	0	6	17	0	11
Herd III	9	0	6	5	0	5
Total	28	0	20	35	0	27
Pregnancy rate ²			71%			77
Not detected (6 days)						
Herd I	45	13	--	53	13	--
Herd II	14	10	--	10	8	--
Herd III	28	9	--	34	17	--
Total	87	32	--	97	38	--
Pregnancy rate ²		37%			39%	

¹Pregnancy rate equals number of animals pregnant ÷ number of cows.

²Pregnancy rates were not significantly different between systems (P>.05).

TABLE 5. ESTRUS IN TWO HERDS OF SUCKLED BEEF COWS RECEIVING THE AI-L-AI-E BREEDING MANAGEMENT SYSTEM

	Herd II (n=47)	Herd III (n=67)	Combined (n=114)
Number observed in 4.5 days (before $\text{PGF}_{2\alpha}$) ¹	8 (17)	8 (12)	16 (14)
Number receiving $\text{PGF}_{2\alpha}$ ¹	39 (83)	59 (88)	98 (86)
Number observed during interval of detection after $\text{PGF}_{2\alpha}$ (hr)			
0 - 12	1	0	1
12 - 24	0	2	2
24 - 36	2	6	8
36 - 48	7	7	14
48 - 60	7	13	20
60 - 72	5	6	11
72 - 84	3	1	4
84 - 96	4	5	9
Total	29	40	69
Total observed in 8.5 days ¹	37 (79)	48 (72)	85 (75)

¹Numbers in parentheses equal percent of total animals.

TABLE 6. COMPARISON OF TWO BREEDING MANAGEMENT SYSTEMS USED FOR 8.5 DAYS OF ARTIFICIAL INSEMINATION¹

	<u>Breeding Management Systems</u>	
	AI-L-AI-E	LL-AI-80
Herd II		
Number of animals	47	45
Number inseminated	37	45
Number pregnant to first AI	25	22
First AI pregnancy rate ¹	68%	49%
Total AI pregnancy rate ²	53%	49%
Herd III		
Number of animals	67	64
Number inseminated	48	64
Number pregnant to first AI	33	29
First AI pregnancy rate	69% ^a	45% ^b
Total AI pregnancy rate	49%	45%
Combined herds		
Number of animals	114	109
Number inseminated	85	109
Number pregnant to first AI	58	51
First AI pregnancy	68% ^a	47% ^b
Total AI pregnancy rate	51%	47%

¹First AI pregnancy rate equals number of animals pregnant to first AI ÷ number of animals inseminated.

²Total AI pregnancy rate equals number of animals pregnant to first AI ÷ numbr of animals in system.

^{a,b}Means with different superscripts within rows are significantly different (P<.05).

TABLE 7. CUMULATIVE CALVING RATES AT VARIOUS STAGES OF THE CALVING SEASON FOLLOWING TWO DIFFERENT BREEDING MANAGEMENT SYSTEMS^a

	<u>Breeding Management Systems</u>	
	AI-L-AI-E	LL-AI-80
Herd II		
Number of animals	47	45
Calving rate:		
in 17 days	64%	76%
in 38 days	72%	84%
in 60 days	83%	91%
Herd III		
Number of animals	67	64
Calving rate:		
in 17 days	57%	56%
in 38 days	78% ^a	92% ^b
in 60 days	90%	94%
Combined herds		
Number of animals	114	109
Calving rate:		
in 17 days	60%	64%
in 38 days	75% ^a	89% ^b
in 60 days	87%	93%

^aCalving rate equals number of cows calved ÷ number in system.

^{a, b}Means with different superscripts within rows are significantly different (P<.05).

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