MONTANA STATE UNIVERSITY

Exogenous hormone therapy to control the postpartum interval in beef cows
by Dallas Blair Foster

A thesis submitted in partial fulfillment of the requirements for the degree of MASTER OF SCIENCE
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Abstract:
Four studies were conducted to evaluate the effects of exogenous hormone treatments on postpartum parameters in the suckled beef cow. In all experiments treatments started about 22 days postpartum and the following three basic treatments were used: PMSG on day 9 with or without a 6 mg progestin ear implant (SC21009, G.D, Searle Co,) from day 0 to day 9 (day 0 = start of treatments) and on day 23 PGF2α in conjunction with the above two treatments. Treatment 3 received only PGF2α, Ovarian activity was evaluated by rectal palpation and blood progesterone in experiments 1, 3 and 4. In the first experiment, eight cows received the progestin implant and either 4000, 2000 or 1000 I.U. of PMSG. Six cows received only one of the three doses of PMSG and four animals received neither the implant nor PMSG. Cows in all treatment groups received 25mg PGF2α and were bred by artificial insemination (Al) following detection of estrus, An ovarian response was evoked following PMSG with and without the progestin implant. Estrus was observed in only one cow following PGF2&apha;. Experiment 2 consisted of 27 cows assigned to 3 groups (Cl, G2 and G3). Gl received a combined injection of 2.5mg estradiol valerate and l,5mg progestin (EV-SC21009) on day 0, the progestin implant and 1000 I.U, of PMSG. G2 received only the implant and PMSG while G3 received no EV-SC21009, implant or PMSG, All groups received 5Omg PGF2a followed by breeding (AI) for 5 days according to estrous detection and by natural service for the remainder of the 45 day breeding season. Average day of conception for the breeding season for Cl, G2 and G3 was 18.2, 9.4 and 23.3, respectively with a significant difference (P<.05) between G2 and G3. Experiment 3 consisted of 27 cows assigned to 3 groups (Cl, G2 and G3), Gl received the progestin implant and 1000 I.U, PMSG. G2 received only the PMSG and G3 received neither the implant or PMSG, All groups were given 5Omg PGF2a followed by breeding (Al) at 72 hours with Hereford and 96 hours with Holstein semen followed by natural service to an Angus bull for the remainder of the 45 day breeding season. Serum progesterone concentrations increased from day 9 to 23 in Gl (P<.05), G2 (P<,01) and G3 (P<.05) with concentrations being greater at day 23 in Gl. A decrease in progesterone concentrations following PGF2α was observed between days 23 and 27 in Gl (P<.05), G2 (P<.01) and G3 (P<.05), Forty cows in experiment 4 were assigned to 5 groups (Gl, G2, G3, G4 and G5). Gl and G3 received the progestin implant and 1000 and 750 I.U, PMSG, respectively. G2 and G4 received only the 1000 and 750 I.U, PMSG, respectively; while G5 received neither the implant nor PMSG. All groups received 5Omg PGF2a followed by a similar breeding regime as that described in experiment 3. Serum progesterone concentrations increased from day 9 to 23 in Gl, G3 and G4 (P<.05). A decrease in progesterone concentrations following PGF2a was observed between day 23 and 27 in Gl and G2 (P<.05) and G3 and G4 (P<.10). These studies demonstrate induced ovarian activity and some of the treatments may be useful in shortening the calving interval.

EXOGENOUS HORMONE THERAPY TO CONTROL
THE POSTPARTUM INTERVAL IN BEEF COWS

by

DALLAS BLAIR FOSTER

A thesis submitted in partial fulfillment
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of

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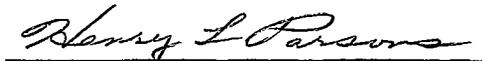
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iii

ACKNOWLEDGMENTS

TABLE OF CONTENTS

Page

INDEX TO TABLES

INDEX TO FIGURES

x

INDEX TO APPENDIX

ABSTRACT

Four studies were conducted to evaluate the effects of exogenous hormone treatments on postpartum parameters in the suckled beef cow. In all experiments treatments started about 22 days postpartum and the following three basic treatments were used: PMSG on day 9 with or without a 6 mg progestin ear implant (SC21009, G.D. Searle Co.) from day 0 to day 9 (day 0 = start of treatments) and on day 23 PGF$_2\alpha$ in conjunction with the above two treatments. Treatment 3 received only PGF$_2\alpha$. Ovarian activity was evaluated by rectal palpation and blood progesterone in experiments 1, 3 and 4. In the first experiment, eight cows received the progestin implant and either 4000, 2000 or 1000 I.U. of PMSG. Six cows received only one of the three doses of PMSG and four animals received neither the implant nor PMSG. Cows in all treatment groups received 25mg PGF$_2\alpha$ and were bred by artificial insemination (AI) following detection of estrus. An ovarian response was evoked following PMSG with and without the progestin implant. Estrus was observed in only one cow following PGF$_2\alpha$. Experiment 2 consisted of 27 cows assigned to 3 groups (G1, G2 and G3). G1 received a combined injection of 2.5mg estradiol valerate and 1.5mg progestin (EV-SC21009) on day 0, the progestin implant and 1000 I.U. of PMSG. G2 received only the implant and PMSG while G3 received no EV-SC21009, implant or PMSG. All groups received 50mg PGF$_2\alpha$ followed by breeding (AI) for 5 days according to estrous detection and by natural service for the remainder of the 45 day breeding season. Average day of conception for the breeding season for G1, G2 and G3 was 18.2, 9.4 and 23.3, respectively with a significant difference (P<.05) between G2 and G3. Experiment 3 consisted of 27 cows assigned to 3 groups (G1, G2 and G3). G1 received the progestin implant and 1000 I.U. PMSG. G2 received only the PMSG and G3 received neither the implant or PMSG. All groups were given 50mg PGF$_2\alpha$ followed by breeding (AI) at 72 hours with Hereford and 96 hours with Holstein semen followed by natural service to an Angus bull for the remainder of the 45 day breeding season. Serum progesterone concentrations increased from day 9 to 23 in G1 (P<.05), G2 (P<.01) and G3 (P<.05) with concentrations being greater at day 23 in G1. A decrease in progesterone concentrations following PGF$_2\alpha$ was observed between days 23 and 27 in G1 (P<.05), G2 (P<.01) and G3 (P<.05). Forty cows in experiment 4 were assigned to 5 groups (G1, G2, G3, G4 and G5). G1 and G3 received the progestin implant and 1000 and 750 I.U. PMSG, respectively. G2 and G4 received only the 1000 and 750 I.U. PMSG, respectively; while G5 received neither the implant nor PMSG. All groups received 50mg PGF$_2\alpha$ followed by a similar breeding regime as that described in experiment 3. Serum progesterone concentrations increased from day 9 to 23 in G1, G3 and G4 (P<.05). A decrease in progesterone concentrations following PGF$_2\alpha$ was observed between day 23 and 27 in G1 and G2 (P<.05) and G3 and G4 (P<.10). These studies demonstrate induced ovarian activity and some of the treatments may be useful in shortening the calving interval.

INTRODUCTION

The human population of the world will double its current number
in about 35 years and nearly triple in 50 years if the present rates of
growth continue. This increase in world population must be accompanied
with a parallel increase in food production. The Food and Agriculture
Organization estimate that about 450 million and possibly as many as a
billion people do not receive sufficient food. To meet the food require-
ments of today and the future we must seek ways to provide for maximum
use of the resources available to us.

Animal products are a major source of the world's diet. In the
United States, livestock produce two-thirds of the protein, one-half of
the fat and one-third of the energy for human consumption. Animal pro-
ducts in developing countries provide 10% of the calories and 20% of
the protein. The United Nations Food and Agriculture Organization
estimates that 20% of the population in these developing countries are
undernourished and 60% are malnourished. Much of this malnutrition,
especially in children, can be attributed to an insufficient protein-
energy source.

An increase in beef production is one of the means for keeping pace
with the world's increasing food needs. Research can lead to improve-
ments in such areas as animal health, nutrition, genetics and reproduc-
tion.

An increase in reproductive efficiency would provide a means in
which to enhance beef production. The most important causes of repro-
ductive failure in the United States have been reported 1) the number

of cows in heat the first 21 days of the breeding season, 2) the number
of cows conceiving at first service and 3) the number of cows losing
calves at or near birth (Wiltbank et al. 1973). The postpartum interval
and the problems associated with the early anestrous beef cow is an area
in which research could lead to improvements in reproductive efficiency.
The use of artificial insemination to enhance availability of quality
semen and recent progress in estrus synchronization have given us a
means of improving both genetic merit and reproductivity performance.

The following study was designed to determine the influence of var-
ious exogenous hormone treatments in decreasing the length of the post-
partum interval in the anestrous beef cow. The objectives of this
study were to investigate the basic postpartum physiology in the
anestrous cow and more specifically to decrease the postpartum interval
to the first fertile estrus and conception. This would lead to a re-
duction in the number of anestrous and low fertility cows present
during the breeding season and thereby increase reproductivity efficiency.

LITERATURE REVIEW

Postpartum Interval

The term postpartum interval may be considered to be that interval
beginning with parturition and ending with a designated event such as
first ovulation, first estrus, completion of uterine involution, first
breeding, or conception (Casida, 1968). In contrast to the more precise
timing of hormonal regulation occurring during the estrous cycle, the
postpartum interval in cattle is generally subject to a greater degree
of variation. There are a number of factors which contribute to this
variation in interval length including lactation (Wiltbank and Cook,
1958; Wagner and Hansel, 1969; Laster et al. 1973a; Bellows et al.
1974; Radford et al. 1978), plane of nutrition (Wiltbank et al. 1964;
Dunn et al. 1969; Oxenreider and Wagner, 1971; Folman, 1973), age
(Wiltbank and Cook, 1958; Wiltbank, 1970; Hill et al. 1972; Rosenberg
et al. 1977), season (Buch et al. 1955; Rosenberg et al. 1977) disease
(Morrow, 1966; Elliot, 1968; Callahan et al. 1971), and dystocia (Rasbech,
1967; Laster et al. 1973b; Foulley et al. 1976).

A better understanding is needed of the anestrous cow and the prob-
lems associated with her return to a normal cyclic hormonal pattern.
This requires an examination of the endocrine physiology and its impact
on the postpartum interval.

Endocrine Physiology

A review of the mechanisms involving the hypothalamus and pituitary
in the control of ovarian function is necessary in order to discuss the

anestrous cow and her return to cyclic ovarian activity. Unfortunately, this system is rather complex and it is still not completely clear how the numerous feedback systems operate in order to compensate for abnormal hormonal secretion patterns. One of the disadvantages involved when approaching this problem is acquiring an _in vivo_ model capable of giving a true representation of what is occurring under natural circumstances. The most common model for physiological studies is the rat, but the ewe is more commonly used for studies of reproductive physiology in larger mammals. There are obvious similarities in reproductive physiology of all mammals but one must be careful not to imply too much when comparing species. The following discussion will review the present understanding in the functions associated with follicular growth, estrogen secretion, ovulation, corpus luteum formation, progesterone secretion and corpus lutuem regression.

Hypothalamic Function

It is now accepted that the hypothalamus controls the release of pituitary hormones via releasing and inhibiting factors (hormones) secreted by neurons in the basal hypothalamus (Gullemin, 1967; Everett, 1969; Convey, 1973; McCann et al. 1973). These hypothalamic releasing factors pass to the pituitary gland by way of a system of portal vessels capable of providing a rapid and efficient transfer of chemical messages between the brain and the pituitary (Gay, 1972). Observations have led to the prevailing theory that the release of pituitary hormones may be

controlled by varing the concentrations of the specific releasing factors

in the blood which flows through the portal system to the pituitary

(Gay, 1972; Convey, 1973). The primary hypothalamic releasing factors

affecting reproduction are luteinizing hormone releasing factor (LH-RF)

and/or follicle stimulating hormone releasing factor (FSH-RF).

There are several possible mechanisms for modification of pituitary

hormone release involved in reproductive function. Convey (1973)

suggests three possibilities: 1) changes in releasing and inhibiting

hormone synthesis and/or release from the hypothalamus; 2) a change in

pituitary responsiveness to the hypothalamic releasing factors such as

changes in hormone storage, releasability or pituitary cell sensitivity;

or 3) a combination of 1 and 2.

Evidence supports the concept of dual sites of target gland feed-

back. A principal site for feedback of gonadal steriod secretion appears

to be at the hypothalamic level as indicated by the ability of hypo-

thalamic lesions to block the stimulatory feedback (Bishop et al. 1972).

Supporting evidence also shows the ability of gonadal steriods to modify

the content of stored gonadotropin releasing factors and prolactin in-

hibiting factor in the hypothalamus (Ajika et al. 1972).

McCann et al. (1973) postulates that stimulation or inhibition of

LH release may occur by actions at both the hypothalamic and pituitary

levels. Evidence from various investigators suggests that steriod

levels may act directly on the pituitary, thus bypassing the hypothalamus,

by sensitizing or preventing sensitization of the pituitary to LH-RF

(Arimura and Schally, 1970; Hilliard et al. 1971). This theory of pitui-

tary control thereby suggests that the influence of the hypothalamus is

not cyclic and regulatory but rather the sensitivity of the pituitary

is variable depending on circulating steriod levels. Increased hormone

release is then a reflection of the increased sensitivity of the pitui-

tary to the tonic secretion of releasing factors by the hypothalamus.

A different control mechanism may be responsible for the release

of prolactin. Much of the evidence has led to the concept that hypo-

thalamic control of prolactin is mediated through an inhibiting factor

(PIF) rather than a releasing factor as seen for gonadotropins. This

is based on the effects of hypothalamic lesions on the release of

gonadotropins and prolactin (McCann and Friedman, 1960; Bishop et al.

1972). Other evidence gives support to the possibility of a prolactin-

releasing factor also being involved in prolactin secretion (Mishkinsky

et al. 1968; Bishop et al. 1972; Mitnick et al. 1973).

Pituitary-Gonadal Relationships

The concept of control of gonadal function by the anterior pituitary

produces the question of what role the gonads play in controlling gonad-

otropin secretion rates. This leads to the discussion of feedback con-

trol mechanisms.

It is generally accepted that ovariectomy causes an increase in

gonadotropin secretion rates in most species including the rat, ewe and

cow (Labhsetwar, 1969; Goding et al. 1970; Roche et al. 1970; Yamamoto et al. 1970; Howland et al. 1971; Snook et al. 1971). This indicates that the gonadal steroids estrogen and/or progesterone in the female are engaged in some type of interacting relationship with the gonadotropins.

When discussing the estrous cycle one can start at any place in time. Since ovulation is the major event associated with the estrous cycle this may be an appropriate place to begin.

It has been known for some time now that ovulation is associated with a large increase in release of luteinizing hormone (LH) from the pituitary gland. In the cow this LH surge in plasma levels is seen at estrus with the LH peak coinciding with, or following the onset of estrus by a few hours, and last for about 8 hours (Hansel and Echternkamp, 1972). Other reports (Swanson and Hafs, 1971) suggest that the LH peak may precede the onset of estrus by approximately 3 hours.

The role of this large LH increase is to bring about ovulation by causing the follicle to rupture and thereby allowing the ovum to be extruded. Ovulation in the cow occurs about 10 to 11 hours following estrus (Thibault and Levasseur, 1975). Follicular rupture is not due to increased intrafollicular pressure but rather to an increase in distensibility (strain/stress) of the follicular wall brought about by the influence of the LH surge (Rondell, 1970). As the atrum enlarges, the follicle wall becomes thinner resulting in a decrease in breaking

strength (Rondell, 1970). It is believed that this increase in distensibility is produced by the action of a collagenase-like enzyme which interferes with the intrafibrillar bonding of collagen in the follicular wall thus decreasing the breaking strength (Rondell, 1970).

It would appear that both estrogen and progesterone play an important part in bringing about the preovulatory surge in LH blood levels. Chenault et al. (1975), Howland et al. (1971) and Henricks (1971a) among others have shown an apparent positive relationship between the rise in estrogen concentration and the large increase in LH levels that occur 3 to 4 days later. Henricks (1971a) also reported that progesterone levels were highest on the fourth day prior to estrus and progressively decreased to vary low levels on the day prior to estrus in the cow. This is similar to changes in progesterone activity described by others (Donaldson et al. 1970; Christenson et al. 1971; Snook et al. 1971; Sprague et al. 1971; Robertson, 1972). Henricks (1971a) also observed that plasma estrogen concentrations were not able to rise about 10 pg/ml, as opposed to the 15 to 25 pg/ml levels measured prior to the LH surge, until progresterone decreased to low levels (below 2 ng/ml). These data indicate a negative correlation between progesterone levels and the LH surge and a positive correlation between estrogen and this large preovulatory LH increase.

This raises the question as to what initiates or controls the mechanism that triggers this preovulatory LH surge? It may be the

declining progesterone concentrations, the rising estrogen levels or a combination of these two factors. Hansel and Echternkamp (1972) were able to show that no significant rise in plasma LH occurs until plasma progesterone concentrations decline to below 1 ng/ml, suggesting that the large LH release is inhibited by higher progesterone levels. This is supported by evidence that progesterone levels declined to less than 50 ng/100ml before the beginning of the LH peak (Snook et al. 1971). Henricks et al. (1971a) reported that a rise in estrogen concentrations greater than 10 pg/ml was not detected until progesterone levels were below 2 ng/ml while Fogwell et al. (1978) observed that with constant basal concentrations of LH, systemic concentrations of estradiol-17B can increase in response to withdrawal of progesterone.

Neither the inhibitory or stimulartory feedback of estrogen on LH is affected by exogenous progesterone treatment in the ovariectomized cow (Howland et al. 1971; Hausler and Malven, 1976).

This combination of high progesterone concentrations and low estrogen and LH secretions appears to inhibit follicular development and ovulation in the postpartum cow. Pituitary availability of gonadotropins does not seem to be the limiting factor since responses to exogenous GnRH administration have been seen from as early as 1 to 21 days postpartum (Cummins et al. 1975; Webb et al. 1977; Kesler et al. 1977; Fernandes et al. 1978; Schallenberger et al. 1978). This would indicate that the circulating progesterone and estrogen concentrations

may be a limiting factor in the initiation of cyclic ovarian activity in the anestrous cow.

During lactation progesterone concentrations are low (less than 1 ng/ml) until resumption of cyclic ovarian activity (Donaldson et al. 1970; Robertson, 1972; Corah et al. 1974; Prybil and Butler, 1978). It has also been seen that the first postpartum cycle is usually preceded by a transcient increase in plasma progesterone concentrations 3 to 5 days before ovulation (Donaldson et al. 1970; LaVoie et al. 1979). Similar results have been observed by Corah et al. (1974), Schams et al. (1978) and Prybil and Butler (1978). Corah et al. (1974) saw a marked elevation in progesterone only in those cows which conceived suggesting that this period of progesterone elevation may be necessary for conception at first estrus. This is supported by Folman et al. (1973) who observed fertility is influenced by progesterone levels in the preceeding estrous cycle. It is not known whether this transcient rise in progesterone prior to the first postpartum ovulation is of adrenal or ovarian origin (Corah et al. 1974; Prybil and Butler, 1978).

A similar situation may exist in the prepuberal heifer. Gonzalez-Padilla et al. (1975a) reported no deficiency in circulating levels of pituitary or hypothalamic hormones two months prior to the onset of puberty in heifers. They also reported two distinct LH peaks shortly prior to puberty, each preceded by a period of elevated progesterone. Swanson and McCarthy (1978) were able to elicite LH response to various

doses of estradiol in prepuberal Holstein heifers at 29±1 weeks of age.
Donaldson et al. (1970) found that plasma progesterone concentrations
at the time of puberty indicated cyclic ovarian activity before the first
observed estrus.

Desjardins and Hafs (1968) determined pituitary FSH and LH in
heifers from birth through puberty and determined that puberty is associ-
ated with a decrease in pituitary LH levels. They also found that
plasma levels were inversely related to pituitary levels indicating an
increase in circulating gonadotropin levels prior to puberty.
Gonzalez-Padilla et al. (1975a) suggests that this establishment of a
mature pattern of LH secretion is not a sudden but a gradual event which
may be mediated by a stepwise increase in progesterone levels with each
elevation serving as a primer for further maturation of the hypothalamo-
pituitary-ovarian axis.

The prepuberal heifer is also similar to the anestrous cow in that
the ovary is receptive to exogenous hormone therapy prior to cyclic
ovarian activity and capable of follicular activity from 11 months up
to puberty (Arije et al. 1969; Neville and Williams, 1973;
Gonzalez-Padilla et al. 1975b).

Hormone Levels During the Bovine Estrous Cycle

With the advent of radioimmunoassays (RIA) in the latter part of
the 1960's an effective and efficient method of measuring levels of
blood hormones has been developed. This has given investigators the

opportunity to monitor hormone levels and develop a better understanding of the events connected with the estrous cycle.

Progesterone

Pope et al. (1969) measured plasma progesterone levels in eight normal cycling Friesian cows and found that levels near the time of ovulation were below 2 ng/ml and rose and fell during ovulation cycles as corpora lutea grew and regressed. Mean peak concentrations for 22 cycles were 9 ng/ml and occurred on an average of 13 days after ovulation. Other investigators have reported peak progesterone concentrations ranging from 3 to 12 ng/ml in dairy cows (Henricks et al. 1971a, Robertson, 1972 and Chenault et al. 1975).

Similar results have been noted in beef cows. Donaldson et al. (1970) observed progesterone concentrations were lowest at estrus (.44 ng/ml) and then increased to a maximum of 6.8 ng/ml at day 14 of the 21 day cycle. Concentrations decreased rapidly during the last 4 days before estrus. This agrees with data reported by Christensen et al. (1971) and Henricks et al. (1971b) but is different from that reported by Sprague et al. (1971) who observed maximum progesterone concentrations on days 9 and 12 followed by a decline thereafter to the next estrous.

Progesterone concentrations in both beef and dairy heifers follow a similar pattern as that seen in the mature cow. Snook et al. (1971) measured progesterone concentrations and observed low levels (<1 ng/ml) following estrus followed by a rise from day 5 to 7 of the estrous cycle.

A progesterone peak (about 4.5 ng/ml) was observed at day 15 to 17 followed by a sharp decline. These results are supported by similar data reported by Hackett and Hafs (1969) and Henricks et al. (1971a).

Pope et al. (1969) suggest that the relatively high progesterone concentrations in mid-cycle are involved in the inhibition of ovulation while the rapidly falling levels of progesterone are more closely associated with impending ovulation. This inhibitory action of progesterone on ovulation has also been reported by Chenault et al. (1975) and is supported by Hackett and Hafs (1969) who at the time of high progesterone concentrations, observed a reduction of hypothalamic LRF (lutenizing releasing factor) which is associated with release of LH and ovulation.

Estrogens

Christensen et al. (1971) measured estrogens during the estrous cycle and observed highest concentrations (176±31.6 pg/ml) at about 24 hours before the LH peak associated with ovulation. They also observed elevated estrogen levels (144±44.2 pg/ml) on days 5 and 6 while levels during the remaining days fluctuated between 98 and 133 pg/ml. Henricks et al. (1971a) reported plasma estradiol concentrations less than 10 pg/ml until the day prior to estrus when concentrations were 15 to 25 pg/ml. Estradiol concentrations greater than 10 pg/ml were not detected until progesterone concentrations were below 2 ng/ml. This differs from Chenault et al. (1975) who observed an increase in estradiol concentrations from 2 pg/ml at 4 days prior to ovulation to 6 pg/ml at 12 hours

before ovulation. This was followed by an abrupt increase to 7.4 pg/ml

at the LH peak with a return to basal levels at 14 hours after the LH

peak. Dobson (1978) reported a similar rise and decline in estradiol

concentrations around the time of the preovulatory LH peak. These data

support the hypothesis that estradiol or a high estradiol to progesterone

ratio is responsible for triggering the preovulatory surge of LH in the

cow (Chenault et al. 1975).

Gonadotropins

Snook et al. (1971) monitored LH levels in cycling heifers and ob-

served basal levels for serum LH of 2 to 4 ng/ml. A preovulatory LH

peak (7 to 50 ng/ml) was observed in every heifer with LH concentrations

declining rapidly following the peak. Christensen et al. (1971) de-

termined LH concentrations in beef cows and observed basal levels of .6

to 1.6 ng/ml with preovulatory LH peaks ranging from 18 to 86 ng/ml.

These elevated levels lasted 12.4±1.56 hours. Other investigators have

reported LH peaks prior to ovulation ranging from 2.6 to 61 ng/ml and

lasting from 6 to 10.5 hours (Sprague et al. 1971, Swanson and Hafs,

1971 and Chenault et al. 1975).

Snook et al. (1971) reported another LH peak 4 to 7 days before

ovulation which was thought to be correlated with growth and atresia

of anovulatory follicles. Snook et al. (1971) also found a positive

correlation between serum LH and progesterone during the luteal phase

(day 3 to 15) which would support the hypothesis that LH is luteotropic

in cattle.

Hackett and Hafs (1969) reported pituitary content of FSH declined from a maximum (450 ug) on day 18 of the cycle to a minimum (122 ug) at estrus and, except for a depression on day 4, increased continuously from estrus to day 18. This agrees with data by Dobson (1978) who observed a significant increase in plasma FSH and LH around the time of estrus. Dobson also reported a second FSH peak which occurred about 24 hours after the dual surge of FSH and LH.

Changes in Hormone Levels During Pregnancy, Prepartum and Postpartum Periods:

Progesterone

Pope et al. (1969) monitored plasma progesterone concentrations in dairy cows during pregnancy and the postpartum period and found concentrations during the last month of pregnancy to be in the 2.5 to 7.5 ng/ml range while dropping to .5 to 3 ng/ml at calving. Ovulatory cycles began at about 20 days postpartum with ovulations without estrus occurring more frequently in the earlier part of the postpartum period when progesterone levels were often quite low. Robertson (1972) observed in dairy cows a gradual decline in progesterone levels over a period of 35 to 70 days prior to parturition reaching a level of less than 2 ng/ml the day before parturition. Following parturition, progesterone levels remained less than .5 ng/ml until the first sign of the resumption of cyclic activity which ranged from 20 to more than 60

days. Others have also reported low concentrations of progesterone in dairy cows from parturition to first postpartum estrus or ovulation (Echternkamp and Hansel, 1973, and Stevenson and Britt, 1979).

In beef cows Donaldson et al. (1970) reported plasma progesterone concentrations during early pregnancy to be similar to luteal phase values (4 to 6 ng/ml) of the estrous cycle. These values declined during mid-pregnancy and then increased to a maximum (7 to 8 ng/ml) at about 240 days and declined 2 to 3 weeks before parturition. Schams et al. (1972) observed a similar increase in progesterone levels at the beginning of pregnancy with levels dropping slightly from day 20 to 40. There was a marked drop in concentrations within two days of parturition. Arije et al. (1974) observed progestin concentrations between 5.2 and 10 ng/ml from 21 to 14 days prior to parturition with concentrations being fairly constant at about 6 ng/ml on the day of parturition. These high progestin levels reported by Arije et al. (1974) are much higher than those reported by others at parturition (Donaldson et al. 1970, Schams et al. 1972 and Corah et al. 1974).

Postpartum progesterone concentrations remained low up to 30 to 39 days following parturition in a group of beef-dairy crossbreeds (Schams et al. 1972). These low postpartum progesterone concentrations have been reported by a number of investigators in beef cattle (Donaldson et al. 1970, Arije et al. 1974 and Corah et al. 1974).

Estrogens

Arije et al. (1974) reported estrogen concentrations the last 20 days prepartum ranging between 870 and 1300 pg/ml with a drop to 500 pg/ml at parturition. Estrogen levels decreased with the next 10 days varying from 122 to 382 pg/ml and throughout most of the postpartum period fluctuated around 200 pg/ml with occasional peaks of 300 to 400 pg/ml. Henricks et al. (1972) observed lower estrogen concentrations (510 pg/ml) 14 days prior to parturition at which time there was a continual rise to 2660 pg/ml at parturition. Stellflug et al. (1978) also noted an increase in estrogens, although not as dramatic, from -158 hours prepartum (399 pg/ml) to parturition (501 pg/ml).

Corah et al. (1974) reported estradiol concentrations peaked at parturition (62.4±5.6 pg/ml), fell sharply to 10.6±1.8 pg/ml one day later and fluctuated between 2 and 5 pg/ml through day 21 postpartum. This is similar to estradiol concentrations reported by Echternkamp and Hansel (1973) who also observed a parallel increase in estrone concentrations at this time.

Gonadotropins

Saiduddin et al. (1966) reported pituitary LH was very low at the time of calving, increased considerable by day 10 and thereafter increased gradually up to day 30 postpartum. Morrow et al. (1968) determined the mean interval from first to second postpartum ovulation in dairy cattle to be significantly shorter than the interval from second

to third ovulation. From this it was hypothisized that low postpartum levels of LH may be responsible for deficient maintenance and early regression of the corpus luteum resulting in a short cycle (Morrow et al. 1968).

Schams et al. (1972) reported LH levels ranged around 1 ng/ml throughout pregnancy while Ingalls et al. (1971) observed no measurable change in serum LH from 30 days before parturition until first estrus following parturition. A number of investigators have reported low LH levels ranging from .5 to 2 ng/ml during the early postpartum anestrous period (Foote, 1971, Echternkamp and Hansel, 1973 and Arije et al. 1974).

Schams et al. (1978) observed a great deal of individual variation in LH profiles with regard to onset of elevations, regularity of patterns and peak values. It was also noted that the preovulatory LH peak values tended to increase with an increase in the number of postpartum estrous cycles. The number of episodic LH peaks and average LH concentration appear to be inversely associated with the interval to first ovulation (Stevenson and Britt, 1979). That is to say, the greater the number of episodic LH peaks, the shorter the interval to first ovulation.

Foote (1971) reported FSH concentrations in early postpartum anestrous cows to follow a trend inverse to the relatively low LH activity seen at this time. This was interpreted to mean a pituitary accumulation of LH is needed in preparation for the LH surge connected with ovulation while a continual, more gradual release of FSH is required

to stimulate follicular development in preparation for ovulation.

The Anestrous Cow and Factors Effecting the Postpartum Interval

A number of factors have been shown to have a distinct effect on the postpartum interval in the cow. Because of their effects on the anestrous period, a brief discussion will be allotted to the major factors involved in lengthening or shortening this period.

Lactation

It is generally acknowledged that lactation lengthens the interval from parturition to first estrus (Graves et al. 1968; Oxenreider, 1968; Short et al. 1972; Smith and Vincent, 1972; Laster et al. 1973a; England et al. 1973, LaVoie, 1975). Graves et al. (1968) reported that the interval in the beef cows from parturition to first estrus was 35 to 54 days shorter for suckled vs nonsuckled cows. Bellows et al. (1974) reported early weaned beef heifers exhibited estrus an average of 20.5 days postpartum compared with 43.2 days for suckled dams. Other results (Radford et al. 1978) indicated that nonsuckled cows experienced regular ovarian cycles 10 to 33 days postpartum while suckled cows failed to have normal cycles until at least 14 weeks postpartum. LaVoie et al. (1979) observed an increase in the postpartum interval from 20 days in non lactating beef cows to 38 days in cows suckled ad libitum.

The amount or type of milking stimulus may also be a factor involving the postpartum interval. Wiltbank and Cook (1958) reported

the interval from calving to first estrus was about 30 days longer in

nursed than in milked Shorthorn cows. Supportive evidence furnished by

Wagner and Hansel (1969) showed the mean interval to the first observed

postpartum estrus was 14 days in a group of milked Holstein cows while

a similar nursed group had not shown estrus by 30 days postpartum.

LaVoie et al. (1979) found an increase, although not significant, in

the postpartum interval from 34 days in cows suckled two times daily

to 38 days in cows suckled ad libitum.

The exact nature as to how lactation mediates its effect on the

postpartum interval is not fully understood. Echternkamp (1978) found

an increased incidence of spontaneous LH release and an increase in

minimum LH concentrations at 30 days postpartum in nonsuckled ovari-

ectomized heifers when compared to nursed groups. Short et al. (1972)

observed lower LH levels in suckled cows while Wagner et al. (1969)

reported follicular activity in nursed animals that did not ovulate sug-

gesting the presence of adequate FSH with an absense of LH available

for ovulation. These data would suggest that lactation suppresses go-

nadotropin secretion and/or synthesis in early postpartum cows

(Echternkamp, 1978).

Failure of suckled beef cows to respond to exogenous estrogen at

6 weeks postpartum gives evidence of failure in positive estrogen feed-

back (Radford et al. 1976). Short et al. (1978) demonstrated that

lactation induced anestrus in the cow may be at least partially mediated

through elevated prolactin levels as a result of suckling. Ratner and

Meites (1964) indicated that in the rat suckling can deplete the hypo-

thalamus of a prolactin inhibiting factor (PIF), thus removing hypo-

thalamic inhibition to prolactin release. Grosvenor (1965) implied

that nursing effects prolactin release in the rat by suppressing PIF

release from the hypothalamus. Han and Moody (1974) found a signifi-

cant difference in prolactin levels in suckled and nonsuckled beef cows

suggesting reduced prolactin secretion as seen in nonsuckled cows may

be necessary for the initiation of estrus. Oxenreider and Wagner (1971)

have revealed a correlation between plasma glucose levels and postpartum

interval and reported that lactation caused lower plasma glucose levels

during the first 56 days postpartum.

Nutrition

The effect of energy level on reproductive performance has been

demonstrated by a number of investigators (Wiltbank et al. 1962; Dunn

et al. 1969; Lamond, 1970; Oxenreider and Wagner, 1971; Folman et al.

1973). A longer interval from calving to first estrus was seen in beef

cows fed one-half the recommended level (low) before calving and the

recommended level (high) after calving compared to cows fed a high

level before and low level of energy after calving (Wiltbank et al.

1962). Dunn et al. (1969) reported a low energy level before or after

calving lengthens the interval from parturition to first estrus.

The nutritional environment both before and after calving is seen

to influence follicular growth and ovulation (Lamond, 1970; Wagner and
Oxenreider, 1971). Oxenreider and Wagner (1971) reported that energy
intake had a significant effect on plasma glucose levels with low glu-
cose levels increasing the interval to first postpartum ovulation.
Dairy cows maintained on a high level of nutrition required fewer in-
seminations per conception, conceived earlier and had a high progester-
one level 23 days earlier than cows on a standard nutrition level
(Folman et al. 1973). These data would support the theory that body
condition as well as energy intake are important factors affecting the
postpartum interval (Wiltbank et al. 1962).

Age

Burke (1954) reported a peak in calf production in 6 and 7 year old
cows with a gradual increase in calf crop percentage up to this age
followed by a gradual decrease through cows 9 years and older. Wiltbank
and Cook (1958) found the interval between calving and first estrus was
shorter between the second through seventh lactation. Young cows nursing
their first calf required 15 to 25 days longer to return to first post-
partum estrus (Wiltbank 1970). Others provide supportive evidence of
younger cows having longer intervals to first estrus and conception
(Hill et al. 1972; Rosenberg et al. 1977).

Season

Wiltbank and Cook (1958) observed no influence of season on repro-
ductive performance. Buch et al. (1955) indicated the interval to first

estrus was shortest in the summer and autumn while Rosenberg et al.

(1977) found the conception rate lower in the summer than in the winter.

The rate of uterine involution was seen to be slower in winter and most

rapid during the spring and summer (Marian et al. 1968). Morrow et al.

(1966) reported no significant affect of season on rate of uterine

involution.

Disease-Dystocia

Uterine infection (metritis) was found to delay the first post-

partum estrus in dairy cows (Callahan et al. 1971). Elliot et al.

(1968) found a rapid decrease in the percent of detectable uterine in-

fections as the interval after parturition increased. They also re-

ported that cows failing to conceive after three or more services had

more leukocytes in the endometrium than did cows conceiving at first

service.

Postpartum diseases such as milk fever, dystocia and retained fetal

membranes slowed ovarian activity in dairy cows (Morrow et al. 1966).

Fewer cows (14.4%) experiencing dystocia were detected in estrus during

a 45 day artificial insemination period resulting in a 15.6% lower con-

ception rate (Laster et al. 1973b). Foulley et al. (1976) reports a de-

creased pregnancy rate after difficult calving without a caesarian sec-

tion while Rasbech (1967) showed a decreased (13 to 14%) conception rate

at first, second or third insemination following the birth of a dead

calf.

Breed

Beef cows tend to have a longer interval from parturition to the first succeeding estrus than dairy cows. Different studies on dairy cows range from 30 to 72 days with comparable figures for beef cows being 46 to 104 days (Wis. Agr. Exp. Sta. Bull. 270, 1968). Some of these differences in postpartum interval length could be attributed to the differences in management schemes between beef and dairy cows since the degree or type of lactation stimulus, as previously reviewed, is known to effect this interval.

Uterine Involution

Several studies indicate that the involutionary state of the uterus does not exert a significant influence on the length of the postpartum periods to first estrus, ovulation and breeding (Foote et al. 1960a; Perkins and Kidder, 1963; Morrow et al. 1968). Reports on the interval from parturition to uterine involution range from 25 to 50 days (Buch et al. 1955; Morrow et al. 1966; Britt et al. 1974a). Factors affecting uterine involution included age, seasons, dystocia, parity, progestagens and GnRH (Buch et al. 1955; Morrow et al. 1966; Marion et al. 1968; Britt et al. 1974b). Factors reported not to affect uterine involution include seasons, production level, cystic follicles, suckling, anemia, ovariectomy, progestagens and estrogens (Morrow et al. 1966; Marion et al. 1968; Wagner and Hansel, 1969; Britt et al. 1974a)

Exogenous Hormone Therapy to Control the Postpartum Interval

Since the early 1960's efforts have been directed by researchers to shorten the postpartum interval by the use of various exogenous hormone treatments. Most of the treatments have been concerned with steroid, gonadotropin, hypothalamic releasing factors and various combinations of these treatments. A prostaglandin, $PGF_2\alpha$, is now recognized as a luteolytic agent in the cow (Lauderdale, 1972 and Inskeep, 1973). This has added another dimension to hormone therapy and may be of increased importance in the future.

Steriod Treatments

The effect of a single injection of progesterone (1 mg/lb body weight) at 14 days postpartum in beef cattle was shown to delay ovarian activity and subsequently the expression of first estrus after calving but did not seem to decrease the interval to uterine involution or affect conception rate (Foote et al. 1960b) Ulberg and Lindley (1960) reported that in cycling beef cows daily injections for 14 days of as little as 12.5 mg progesterone per day could inhibit both estrus and ovulation. This daily progesterone administration was also shown to have a depressing effect upon pregnancy rate of animals inseminated during the first estrus after treatment, with higher doses being even more detrimental. Marion et al. (1968) were able to show in dairy cows that higher doses (30 mg/day) of progesterone significantly increased the interval to uterine involution. Silicone rubber implants impregnated with

progesterone were implanted in the side of the neck in beef cows and left in place for 21 days (Maher et al. 1973). The implant synchronized estrus and ovulation but tended to lower conception rates following implant removal. This effect of lowered fertility following mating at first estrus seems to be predominant in a number of progesterone regimes including melengestrol acetate (Hill et al. 1971), impregnated silastic coils (Roche, 1976), progesterone implants (Chupin et al. 1975) and progesterone injections (Ulberg and Lindley, 1960).

Lamond et al (1971) suggested that progestins such as melengestrol acetate (MGA) may cause suppression of ovarian function in the cow by altering the precise regulatory mechanism exerted by the hypothalamus on secretion of gonadotropins, resulting in an abnormal release of gonadotropins. According to this view, optimum fertility would follow a dose of progestin which causes the least alteration to the normal follicular pattern during treatment. Chupin et al. (1975) found that maximum fertility with a progestin implant (SC21009) resulted from treatments that involved a high dose (12 mg) for a short period of time (7 days).

Because of this fertility problem involving progestagens, a great deal of investigation has been directed towards the use of estrogens used in combination with progesterone to provide an effective treatment in enhancing reproductive efficiency. An injection of .5 to 10 mg estradiol benzoate following 14 daily injections of progesterone

was shown to reduce much of the variation in onset of estrus due to pro-
gesterone administration (Ulberg and Lindley, 1960). Saiduddin et al.
(1968) reported effects of exogenous progesterone and estradiol at vari-
ous stages postpartum in beef cows. Their results indicated that cows
given estradiol alone or following progesterone treatment resumed ovarian
activity earlier after parturition than did untreated or progesterone
only treated cows. Treatment given earliest after parturition (5 to 15
days) caused earliest ovulations but cows treated midpostpartum (14 to
24 days) had shortest intervals to conception. It was postulated that
progesterone tended to lessen the influence of estrogen in hastening
estrus and ovulation, but may have increased the fertility of the estro-
gen treated cows since conception occurred earliest in cows given both
hormones. This agrees with similar data described by Brown et al. (1972)
who fed dihydroxyprogesterone acetophenide (DHAP) daily for 9 days (120
mg/day) but gave a 5 mg estradiol valerate injection on the second day
of treatment. Brown's group found that animals who started treatment in
the 30 to 35 day postpartum interval had the highest first service con-
ception rate when both hormones were administered. Data provided by
Hill et al. (1972) showed that progesterone administration in the form
of 6-chloroΔ^6-17 acetoxyprogesterone (CAP) fed daily from parturition
for 10, 20, 30 or 40 days followed by a .5 mg estradiol-17β injection
resulted in no improvement in the interval to first estrus or conception.
Britt et al. (1974a), starting MGA feedings at 21 days postpartum in

dairy cattle followed by 500 ug estradiol benzoate after 14 days of MGA, found there was no effect of treatment interval to first ovulation but the interval to first conception and services/conception were lower for treated cows. In this last particular case estradiol benzoate after MGA produced similar results as the MGA administration alone.

When reviewing steriod therapy in the anestrous cow it might also be of value to look at estrous synchronization using the cycling cow. In both the anestrous cow and the estrous synchronized cow, control of the estrous cycle is desired, thus, a treatment regime in one may give insight to an effective treatment in the other. Although normal cyclic endocrine control has not been completely reestablished in the anestrous cow, a means of providing a fertile estrus is sought for both models.

Corah et al. (1974) observed that a period of progesterone elevation prior to first estrus may be necessary for conception to occur. This is supported by Folman et al. (1973) who concluded that a high concentration of peripheral progesterone (greater than 4 ng/ml) at the peak of the luteal phase of at least one estrous cycle before insemination was positively associated with conception. Snook et al. (1971) suggested that declining progesterone levels may be one factor responsible for the pre-ovulatory LH surge. With this in mind Folman et al. (1973) postulated that this large drop in progesterone concentrations found in cows that conceived after first insemination may cause the release of greater quantities of gonadotropins affecting ovulation and estrogen production.

Exogenous progesterone may be necessary in the anestrous cow in order to acquire a progesterone "build up". An entirely different function is associated with exogenous progesterone in the synchronized cow. In this case it acts to inhibit estrus and ovulation (Hill et al. 1971a; Roche, 1974; Kinder and Ellington, 1974). The similarity exists between the two uses of progesterone therapy in the fact that a change in the pattern and secretion rate of endogenous hormones may occur (Hill et al. 1971; Henricks et al. 1973a; Hansel et al. 1975).

The stage of the estrous cycle at which treatments are administered in synchronized cows appears to be a factor in determining onset of estrus and affects on fertility (Hill et al. 1971; Roche, 1974; Humphrey et al. 1977). Roche (1974) found that estrous response was higher in animals that received progesterone implants during the luteal phase of the estrous cycle but Hill et al. (1971) observed that synchronization of estrus was better in animals in which MGA treatment was initiated on day four of the cycle. Humphrey et al. (1977) indicated that the presence of a palpable corpus luteum (CL) at initiation of treatment had no effect on the synchronized estrus but pregnancy rates were higher if a CL was present.

The difficulty in interpreting data concerning these types of hormonal treatments lies in all the variations in treatments that can arise when comparing results. This includes the type and dose of progestin administered, the way in which it is applied, the length of time the

animal is exposed to it and the stage of the cycle or postpartum period
in which treatment is initiated. In addition to this, the use of supple-
mental hormones such as various estrogens, gonadrotropins and hypothal-
amic releasing factors compound the number of possibilities that exist.
To this one might add another very important factor and that is the time
interval from the termination of the postpartum or synchronized treatment
to the time of insemination.

Gonadotropic Therapy

The use of gonadotropins in stimulating ovarian activity has been
demonstrated by a number of investigators (Oxenreider, 1968; Bellows
et al. 1969; Chupin et al. 1975; Mulvehill and Sreenan, 1977; Archbald,
1978; Echternkamp, 1978). Pregnant mare's serum gonadotropin (PMSG),
which is known to mimic FSH activity, has been shown to be an effective
agent in stimulating follicular development in the cow (Lamond, 1970;
Wagner et al. 1973; Henricks et al. 1973b; Gengenbach et al. 1978;
Henricks and Hill, 1978). In the anestrous cow, PMSG treatments have
produced varying amounts of success in effecting ovarian activity.
Oxenreider (1968) maintained that the interval from parturition to first
estrus and ovulation were shortened with the use of 2500 I. U. PMSG
followed by 2000 I. U. of human chorionic gonadotropin (HCG) 4 days
later in the early postpartum cow. Phelps et al. (1976) were able to
shorten the interval to first estrus in 45 day postpartum beef cows
using a 2000 I. U. dose of PMSG. No other intervals were significantly

affected although there was a slight decrease in the intervals to first

ovulation and conception. Improvement in fertility was detected in post-

partum beef cows with a 750 I. U. dose of PMSG following a short-term

(9 days) progestagen treatment (Mulvehill and Sreenan, 1977). Similar

results were obtained earlier by Chupin et al. (1975) using a 800 I. U.

dose of PMSG. Brown et al. (1972) found that progesterone and estrogen

therapy used in conjunction with 1000 I. U. of PMSG, followed by 750

I. U. HCG at time of insemination did not decrease intervals to estrus,

ovulation or conception.

One of the problems concerning PMSG is the great amount of variation

associated with dose responses. Lamond and Gaddy (1972) using PMSG

doses between 1500 and 2500 I. U. in cycling beef cows showed responses

varying from 1 to 28 ovulations with progesterone concentrations ranging

from 1 to greater than 180 ng/ml. This agrees with similar data by

Gengenbach (1978) illustrating that higher doses (2000 I. U. PMSG) re-

sulted in greater variation in response (1 to 19 ovulations).

It has been suggested that the difficulty in using PMSG is its long

half-life (5-6 days; Menzer and Schams, 1979) which might be expected to

interefere with the neuroendocrine mechanisms for ovulation (Lamond, 1970).

On this assumption one might interpret the higher doses of PMSG to mean

a longer exposure of the ovary to the gonadotropic stimulation resulting

in a greater degree of interference with the neuroendocrine control of

the estrous cycle. Lamond and Gaddy (1972) contend that crowding of

CL's in an ovary as a result of higher PMSG doses, may affect local mechanisms relating to CL maintenance. They suggested that the uterus may possibly be affected by the greatly elevated progesterone concentrations, resulting in premature initiation of CL regression.

In order to create an ovulation rate and progesterone concentrations closer to physiological levels lower doses of PMSG have been tested. Henricks et al. (1973b) reported that a lower dose of PMSG (1600 I. U.) induced ovulation of as many fertile ova per heifer as the higher dose (3200 I. U.) while causing less of a disturbance in the endocrine system. Rajamabedran et al. (1976) also indicated that there was no significant difference in ovarian response between doses of 1000 and 2000 I. U. of PMSG in heifers. Ovarian responses have been reported with lower doses of 500 I. U. (Gengenbach et al. 1978), 750 I. U. (Mulvehill and Sreenan, 1977), 800 I. U. (Chupin et al. 1975) and 900 I. U. of PMSG (Lamond, 1970). Echternkamp (1978) was able to evoke stimulated estrogen secretion and subsequent LH surge in anestrous beef cows (42 days postpartum) with a 750 I. U. dose of PMSG.

Human chorionic gonadotropin (HCG) has biological activity similar to LH and appears to be responsible for maintenance of the corpus luteum of pregnancy in women (Niswender et al. 1972). Moody and Hansel (1967) have demonstrated HCG to be luteotropic in the cow. A 1000 I. U. dose of HCG in conjunction with progesterone therapy and CL removal resulted in an increase in CL size with 2000 and 4000 I. U. doses producing

additional growth responses (Veenhuizen et al. 1972). Use of a 21 day

progesterone treatment followed by 6000 I. U. of HCG showed a positive

affect on estrus and ovulation in mid to late (56 to 83 days) postpartum

beef cows (Maher et al. 1973). Others have also shown that HCG used in

conjunction with steriod therapy have resulted in improved pregnancy rates

(Wagner et al. 1973; Brown et al. 1973). Wagner et al. (1973) hypothe-

sized that HCG may increase pregnancy rate by 1) synchronizing ovulation

relative to insemination and 2) increasing luteal function during the

first few days following insemination. Wettemann and Hafs (1973) re-

ported that HCG had little effect on serum LH concentrations or fertility

while Kinder and Ellington (1974) showed that the addition of HCG to

their progestogen treatment did not produce any marked improvement in

estrous synchronization and may have had a detrimental effect.

Hypothalamic Releasing Hormones

Response to hypothalamic releasing hormones in the postpartum cow

have been quite variable. In lactating Holstein cows repeated doses of

gonadotropin releasing hormone (GnRH) appeared to initiate estrous cycles

when administered to cows with ovarian follicular cysts (Kittok et al.

1973). The use of a GnRH implant (100 ug) placed subcutaneously in the

ear of 14 day postpartum dairy cows resulted in a shorter interval to

first ovulation but did not effect the interval to first estrus (Britt

et al. 1974b). Webb et al. (1977) reported that treatment of early

postpartum beef cows with an injection of 500 ug GnRH followed by another

injection of GnRH after the first induced luteal phase appeared to ini-
tiate normal cyclic activity. Gonadotropin releasing hormone was found
to have no positive effect on pregnancy rate when administered following
a progestagen treatment in beef cattle (Roche, 1976).

Reports of response to GnRH administration are also quite variable.
Webb et al. (1977) reported response to luteinizing hormone-releasing
hormone (LH-RH) was reduced up to 20 days postpartum while Fernandes
et al. (1978) found an LH response restored between 10 and 20 days post-
partum. Kesler et al. (1977) indicated pituitary responsiveness to GnRH
was regained by 7 or 8 days postpartum and both Cummins et al. (1975) and
Schallenberger et al. (1978) provided evidence that the immediate post-
partum period in the cow is capable of giving an LH release similar to
that of normal estrus. This wide range of response patterns for LH
release with GnRH after parturition might be one of the reasons for
the individuality in the initiation of a new estrus in postpartum
cattle.

$PGF_2\alpha$

It is known that the corpus luteum plays a major role in controlling
the length of the estrous cycle and ovulation through its secretory
product, progesterone. The control of luteal function is thereby a
means of regulating the estrous cycle. This reasoning led to the search
of a uterine luteolyic factor capable of causing chemical regression of
the CL.

Prostaglandin $F_2\alpha$ ($PGF_2\alpha$) was initially tested by uterine infusion in rats (1 mg/kg/day) on days 5 and 6 of pseudopregnancy (Pharriss and Wyngarden, 1969). They saw a dramatic decrease in the progesterone content of the ovaries on day 7 and a shortening of pseudopregnancy to 7 days from the normal 14 day period. Pharriss et al. (1970) postulated that $PGF_2\alpha$ was a venoconstrictor which is released from the uterus and thereby reduces blood flow to the ovary to cause luteolysis. Pharriss et al. (1970) tested this hypothesis by cannulating the utero-ovarian vein in a group of rabbits. They found a reduced blood flow following a 1 or 2 mg dose of $PGF_2\alpha$. Other possible modes of action of $PGF_2\alpha$ includes a direct lytic effect on the steroidogenic cells (Okamura et al. 1972; Koering et al. 1973) and interference with the hormonal support of the corpus luteum (Jacobson et al. 1974; Hichens et al. 1974).

Luteolysis by $PGF_2\alpha$ has been shown in a variety of species including rats, hamsters, sheep and cattle (Pharriss and Wyngarden, 1969; Labhsetwar, 1971; Goding et al. 1972; Louis et al. 1972; Lauderdale, 1972). Exogenous $PGF_2\alpha$ is known to induce luteal regression in cattle with a functional CL during days 5 through 18 of the estrous cycle (Inskeep, 1973). Prostaglandins in cattle have been utilized primarily with estrous synchronization work and to some degree with superovulation (Archbald, 1976; Gengenbach, 1978; Henricks and Hill, 1978) and the postpartum cow (Manns and Richardson, 1976; Radford et al. 1976; Rovira et al. 1978).

The sequence of events after induction of luteolysis with $PGF_2\alpha$

seems to be a rapid follicular growth and secretion of estradiol-17β

with the resulting expression of estrus (Archbald, 1976). It appears

that if estrus is to occur, follicles larger than 10 mm must be present

on the ovary, even though CL regression has occurred (Archbald, 1976).

This has led to the use of PMSG in association with $PGF_2\alpha$ treatments.

Gengenbach et al. (1978) using Holstein heifers was able to show a tight-

ly synchronized estrus when a low dose (500 I. U.) of PMSG was employed

at the same time or 12 hours prior to $PGF_2\alpha$. Estrus tended to be later

in animals receiving higher doses (1200 and 2000 I. U.) with a greater

variation in onset also. They concluded that heifers returning to estrus

2 to 4 days following PMSG or $PGF_2\alpha$ tended to have lower and more uni-

form ovulation rates than heifers returning to estrus after 4 days. In

heifers approaching puberty a 1750 I. U. dose of PMSG followed by 30 mg

of $PGF_2\alpha$ 18 days later resulted in 15% of the heifers in estrus within

6 days after $PGF_2\alpha$ treatment. Henricks and Hill (1978) administered to

beef heifers PMSG (1600 I. U.) and $PGF_2\alpha$ together during the mid (day

9 or 10) or late (day 16 or 17) luteal phase of the estrous cycle.

They also gave to another group of heifers PMSG at mid and late luteal

phase followed by $PGF_2\alpha$ two days later. They found a suppression

of the effects of PMSG when $PGF_2\alpha$ was given the same day. There

was no effect of treatments on pregnancy rate. Chupin and Pelot

(1978), using dairy cows, administered steroid and PMSG therapy.

with and without a prostaglandin analog at the end of the treatment
period. Their results showed an increased calving rate with the prosta-
glandin analog.

A number of exogenous hormones have been used in the postpartum cow
in conjunction with prostaglandins including PMSG, FSH, HCG, GnRH,
estrogens and progestins (Radford et al. 1976; Manns and Richardson, 1976;
Rovira et al. 1978; Chupin and Pelot, 1978). All have had varying
amounts of success with no one producing a satisfactory therapeutic
model for the problems involved in the anestrous cow. The use of these
hormone treatments and their ability to produce a fertile estrous cycle
is the primary problem to be encountered in the postpartum cow.

MATERIALS AND METHODS

Four experiments were conducted to determine the effects of various
exogenous hormone treatments on the anestrous postpartum interval in
suckled beef cows. This interval is characterized by low progesterone
serum levels as a result of little or no follicular activity occurring
in the ovaries. The treatments were designed to stimulate ovarian ac-
tivity and initiate the resumption of a normal hormonal pattern needed
in order for conception to occur. In three of the four experiments
ovarian activity was evaluated by rectal palpation and blood samples
taken throughout the experimental period.

Experiment 1

Eighteen suckled beef cows ranging from 18 to 24 days postpartum
(20.44 average) were randomly allotted to seven treatment regimes
(figure 1). Cows ranged from 3 to 6 years of age and calved between
March 7 and March 29, 1978. All animals were maintained on the same
prepartum and postpartum nutrition scheme.

Eight cows received a 6 mg silastic progestin implant (G. D. Searle
Co.) subcutaneously in the ear on day 0 (day 0 = start of treatment).
Implants were removed on day 9 followed by an injection (im) of either
4000, 2000 or 1000 I. U. of PMSG. Two cows received the 4000, 3 cows
the 2000 and 3 cows the 1000 I. U. dose of PMSG at the time the implant
was removed. Six cows received no progestin implant but did receive
PMSG on day 9 of the treatment schedule. This included 2 cows receiving
4000, 3 cows 2000 and 1 cow 1000 I. U. doses of PMSG. Four animals

served as controls and received neither the implant nor PMSG. All the treated animals and the controls were given (im) a 25 mg dose of $PGF_2\alpha$ on day 23. The cows were observed twice daily for estrus. Following the $PGF_2\alpha$ injection, a sterile bull equipped with a paint marking harness was also used to aid in detecting estrus. The cows were bred by artificial insemination within 8 to 22 hours following estrous detection.

Blood samples (5 to 10 ml) were taken via tail vein on days 0, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27 and 41 of the treatment period. Rectal palpation, to evaluate ovarian activity, was conducted on the same days the blood samples were taken. Blood samples were stored at $4^\circ C$ on the day of collection followed by centrifugation and storage of serum at $-25^\circ C$ the next day.

Progesterone concentrations were measured in serum samples by radioimmunoassay techniques. All serum samples for a particular cow were done in the same assay with 3 cows in each assay. Treatments were randomized throughout the assays in order to minimize assay variation between treatments. A high and low value serum progesterone standard was included at the beginning and end of each assay in order to account for intra- and inter-assay variations.

Experiment 2

This experiment was conducted at the Montana State Prison Ranch, Deer Lodge, Mt., on a group of cows that calved in the latter part of the calving period (April 16 to May 22, 1978). The cows ranged from 3