The Bovine Estrous Cycle and Synchronization of Estrus

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Estrous synchronization gives many beef cattle producers the opportunity to capture the economic benefits of artificial insemination (AI). Because AI involves a substantial investment of labor and time, most commercial farms or ranches will not utilize this technology unless this investment can be confined to a period of less than 5 to 7 days. To make the labor requirements of AI compatible with modern beef cattle breeding, the estrous cycle must be synchronized so that a high percentage of treated females show a fertile, closely synchronized estrus. The synchronization of cattle can be achieved by the use of progestogens,[1] progestogen-prostaglandin combinations,[2] prostaglandins alone,[3] progestogen-estrogen combinations,[4,5] and gonadotropin-prostaglandin combinations with or without progestogens.[6]

In order to understand how each of these hormones, and the programs that have been developed around them, work in individual animals and on a herd basis, one must review the physiology of the bovine estrous cycle.

Bovine estrous cycle

The modal length of the estrous cycle is 21 days for mature cows and 20 days for heifers. The cycle is divided into four periods: estrus, metestrus, diestrus, and proestrus (Figure 1).

Estrus is characterized as the time period when the heifer exhibits sexual desire and acceptance of the male by standing to be mounted. This period lasts from 6 to 30 hours, with 20 hours being the average length. During estrus, the vaginal and cervical mucus production is greatly increased and mucus may be visible hanging from the vulva or wrapped around the tail. The corpus luteum (CL) has been lysed prior to this period; therefore, progesterone production (and subsequent blood level) is very low. Luteinizing hormone (LH) spikes to a high level during estrus, which initiates ovulation. And, estrogen levels are decreasing from the high levels that were reached just prior to estrus.

Metestrus lasts 3 to 5 days. Ovulation occurs during metestrus, about 10 to 15 hours after the end of estrus. During this period, the CL is undergoing early development. Observant producers may notice a slightly bloody vulvar discharge from some heifers due to the rupture of small vessels in the endometrium. Progesterone levels are still low, but increasing slightly during metestrus. This is because the CL is small and does not have the capacity to produce large amounts of progesterone at this stage of development. During metestrus, prostaglandin $F_{2\alpha}$ is not effective at lysing the immature, growing CL and causing a return to estrus; however, large doses of estrogen are effective luteolytic agents during metestrus.

Diestrus, the period of the CL, lasts about 12 days. The CL is producing increasing amounts of progesterone during the early days of diestrus, as the capacity for steroid production increases as the CL matures. As diestrus progresses, concentrations of progesterone in blood plateau. During diestrus, $PGF_{2\alpha}$ will lyse the CL and initiate a return to estrus, whereas high doses of estrogen will not.

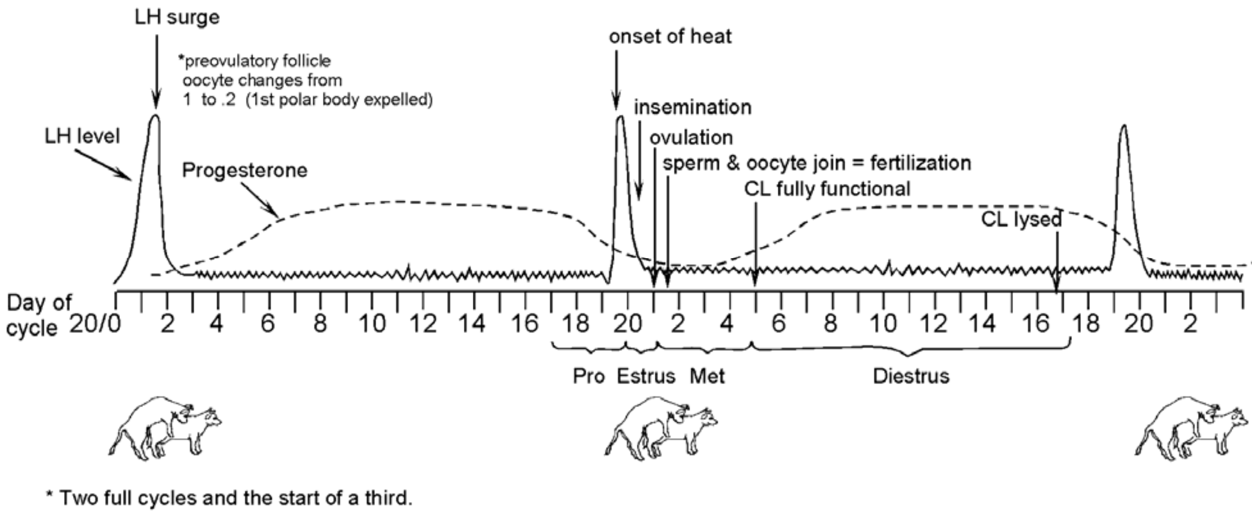

Figure 1. Schematic of stages of the estrous cycle, serum progesterone concentrations, and serum luteinizing hormone (LH) concentrations .

Proestrus lasts about 2 to 3 days and is characterized by regression of the CL and the final growth phase of the ovulatory follicle. As progesterone levels in the blood decrease, LH and estrogen positively feed-back on one another so that a rapid increase in estrogen production by the ovulatory follicle occurs, increasing blood concentrations. The CL is already undergoing regression at this stage; therefore, treatment with $PGF_{2\alpha}$ would not affect the animal’s normal return to estrus.

Hormones controlling the estrous cycle

The hypothalamus controls the release of pituitary hormones by releasing small peptide hormones that travel down short blood vessels from the hypothalamus to the pituitary (Figure 2).

The hypothalamic hormone, gonadotropic releasing hormone (GnRH) causes the pituitary to release luteinizing hormone (LH) and follicle stimulating hormone (FSH). Other hypothalamic hormones either inhibit or induce the release of additional pituitary hormones (growth hormone, ACTH, TSH, MSH and prolactin). These hormones have some affect on reproduction, but we will focus on FSH and LH because they more directly regulate the estrous cycle.

The hypothalamus is affected by steroid hormones secreted by ovarian structures, the adrenal glands, and the placenta. We generally think of the steroid hormones estrogen and progesterone as inhibitors of the hypothalamic secretion of GnRH, but a baseline level is necessary or stimulatory to GnRH secretion.

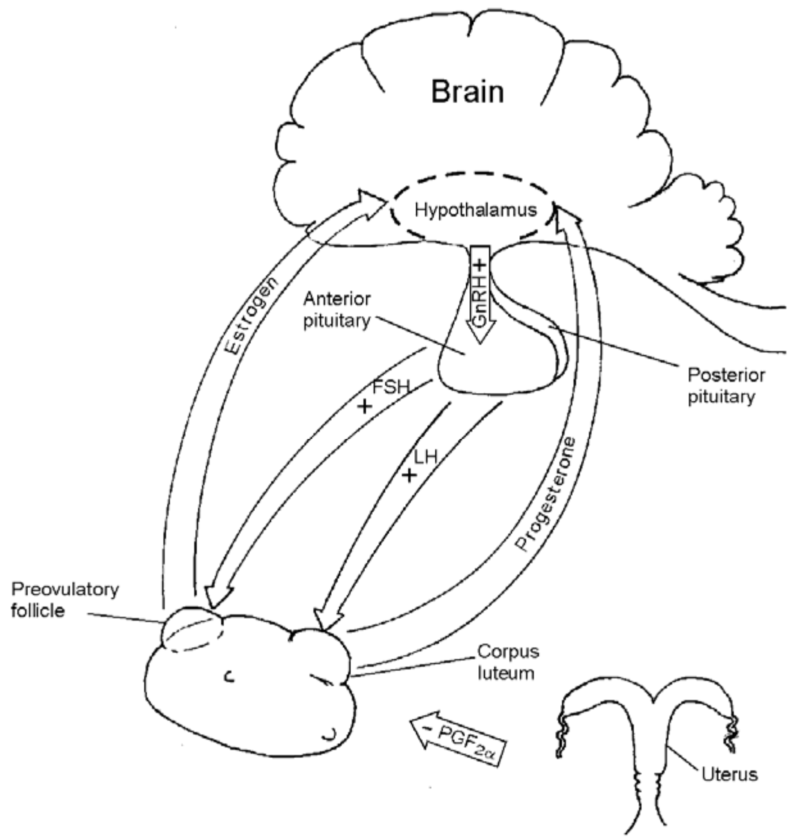

Figure 2. Interaction of hypothalmic, anterior pituitary, ovarian, and uterine hormones on the control of reproduction.

The anterior pituitary lies directly below the brain. GnRH secreted by the hypothalamus causes cells in the anterior pituitary to secrete FSH and LH. FSH stimulates the maturation of secondary follicles to tertiary follicles and stimulates the production of estradiol by the graafian follicle. LH is necessary for the maturation and estrogen production of tertiary follicles. LH is also necessary for the maintenance of the CL and stimulates the production of progesterone by the CL.

Progesterone, produced by the CL, prepares the uterus for entry of the fertilized egg (day 5 of pregnancy) and "quiets" the uterus to maintain pregnancy (inhibits contractions). High levels of progesterone (those found during diestrus and pregnancy) override the effect of estrogen to prevent estrus behavior.

Prostaglandin $F_{2\alpha}$ and oxytocin, produced by the uterine endometrium and ovary respectively, are necessary for luteolysis.

Commonly used commercially available hormones

Cystorelin®, Factrel®, and Fertagyl® - GnRH
Acts to increase the release of FSH and LH from the anterior pituitary gland. The increased LH concentration causes ovulation and luteinization of most dominant or large growing follicles. As a result, a new follicular wave is initiated in all cows about 3 days after the injection.

PMSG: Pregnant Mare Serum Gonadotropin (aka eCG)
Produced by the deciduate cells of the equine placenta. This hormone exhibits predominantly FSH activity but also some LH activity, and is used in the superovulation of cattle.

hCG: Human Chorionic Gonadotropin
Produced by chorionic epithelial cells of the human placenta. This hormone exhibits predominantly LH activity but also some FSH activity, and is used in the superovulation of cattle.

Progesterone - component of CIDR® system
Administered in a controlled-release vaginal insert that releases progesterone over a 7-day period. After 7 days the insert is removed. The progesterone from the devise acts like natural progesterone from the CL: it prevents the decrease in blood levels of progestogens after the CL is lysed naturally on day 17 of the cycle, thereby preventing the increase in LH and estrogen that cause maturation of the ovulatory follicle, ovulation, and estrus.

Melengestrol acetate - MGA® - a synthetic progestogen
When administered in the feed at .5 mg / head / day, this synthetic progestogen mimics progesterone produced naturally by the CL. It does not affect the lifespan of the CL. In other words, the CL is still lysed naturally on day 17 of the estrous cycle. However, as long as MGA is present in the feed at the dosage of .5 mg, the blood level of progestogen is high enough to prevent the spike in LH necessary to initiate ovulation and to prevent estrogen concentrations to increase to the level necessary to initiate estrous behavior.

Lutalyse®, Estrumate®, ProstaMate® and In Synch® - Prostaglandin $F_{2\propto}$ or PGF-like
These products are used primarily to synchronize estrus in cattle and to abort feedlot heifers. They act by lysing the CL (only during diestrus), which causes a rapid decline in progesterone production by the CL.

Follicular waves

A relatively new discovery in reproductive physiology is that follicular growth is not continuous in the bovine, but occurs in waves (2 to 4 waves per cycle; Figure 3). Each wave begins when the dominant follicle in the previous wave gains maximal size, at which time numerous small follicles begin a period of rapid growth. From this group of follicles, one follicle is allowed to grow to a much larger size than the others. This large follicle is called the dominant follicle, because it has the ability to regulate and restrict the growth of the smaller follicles. A few days after reaching maximum size, the dominant follicle begins to degenerate and die. As the dominant follicle degenerates, its ability to restrict the other follicles is reduced; therefore, a new follicular wave in initiated. A consequence of this dynamic process is that follicles of all sizes, including at least one large follicle, exist on each day of the estrous cycle. The large follicle that eventually ovulates is identifiable on the ovary only 48 hours before estrus.

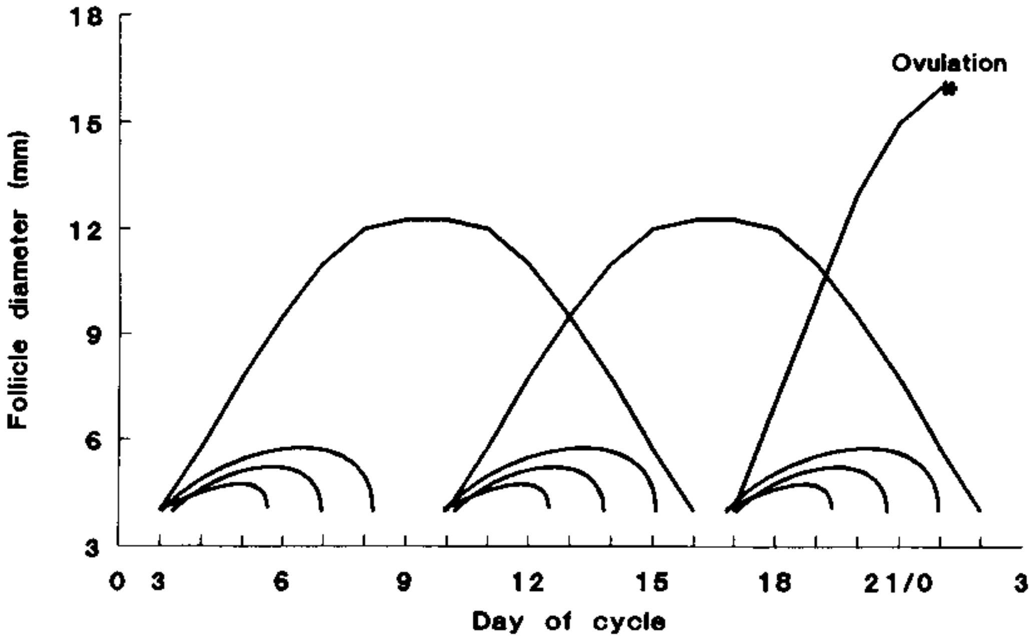

Figure 3. Follicular waves in the bovine

Table 1. Characteristics of a 3-wave estrous cycle

Dominant follicle	Wave 1	wave 2	wave 3
Day wave begins	2	9	16
Maximum size	12 mm	10 mm	13 mm
Persistence	16.9 d	13.1 d	5.9 d

Summary

Synchronization of fertile estrus in heifers can be accomplished with progestogens, combinations of progestogens and prostaglandin $F_{2\alpha}$, prostaglandin $F_{2\alpha}$ alone, and combinations of gonadotrophin-releasing hormone and prostaglandin $F_{2\alpha}$. Advantages and disadvantages of each system as well as the management capabilities and expectations of the producer should be considered when determining the most appropriate estrous synchronization product or protocol.

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