Effects of suppressing plasma FSH on ovarian follicular dominance in cattle

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The importance of FSH during development of the dominant follicle of the first wave of follicular growth in cattle was assessed by injecting heifers twice daily with 20 ml saline ($n = 6$) or 20 ml charcoal-extracted bovine follicular fluid (bFF; $n = 10$), containing inhibin, on days 6 and 7 of the oestrous cycle. All animals received a luteolytic dose of PGF_{2α} on day 8. The interval to oestrus after PGF_{2α} in controls was 2.6 ± 0.2 days. Five of ten bFF-treated heifers exhibited oestrus at the same time as controls (2.7 ± 0.1 days), whereas time to oestrus in the remaining five bFF-treated heifers was significantly longer (6.8 ± 0.6 days; $P < 0.05$). Treatment with bFF suppressed plasma FSH during the 48 h injection period ($P < 0.05$). Concentrations of FSH were not different in bFF-treated animals that did not display delayed oestrus compared with those in animals that exhibited delayed oestrus. In controls, the dominant follicle of the first wave continued growing during treatment and ovulated after injection of PGF_{2α}. In all ten bFF-treated animals, growth of the dominant follicle of the first wave was arrested during the treatment period. In bFF-treated animals that did not exhibit delayed oestrus, the dominant follicle resumed growth after luteolysis and ovulated. In bFF-treated animals that displayed delayed oestrus, the dominant follicle regressed after luteolysis and the ovulatory follicle was selected from a newly recruited (second) wave of follicular growth. Maximal increases in concentrations of oestradiol in plasma reflected preovulatory follicular development and occurred at the time of oestrus, 2 or 3 days after PGF_{2α} injection in saline- and bFF-treated heifers that did not display delayed oestrus, and 5–8 days after PGF_{2α} in animals in which oestrus was delayed. No differences in concentrations of plasma LH or progesterone were detected between groups. Arrested growth of the dominant follicle of the first wave, associated with suppressed concentrations of basal FSH, suggests an important role for FSH during ovarian follicular dominance in cattle.

Introduction

The use of ultrasound imaging has clearly elucidated the pattern of ovarian follicular growth in cattle. Follicular development is characterized by the recruitment of two or three successive cohorts of follicles during each oestrous cycle. From each cohort, a single follicle is selected to develop into a large dominant follicle (Savio *et al.*, 1988; Sirois and Fortune, 1988; Knopf *et al.*, 1989). Although experiments with sheep have provided evidence that basal levels of gonadotrophins are required for follicular recruitment (Dufour *et al.*, 1979; McNeilly *et al.*, 1986; Driancourt *et al.*, 1987), the importance of gonadotrophin support during later stages of follicular maturation has not been addressed definitively.

One hypothesis about the mechanism by which follicular dominance is achieved suggests that in the presence of basal gonadotrophin concentrations, a single follicle continues to

grow and mature because it acquires increased sensitivity to FSH, while further development of other follicles in the same cohort with less sensitivity to FSH is inhibited (Baird, 1987). Receptors for FSH are present on bovine granulosa cells of oestrogen-active follicles on day 3 of the oestrous cycle, and there are more LH receptors on theca and granulosa cells of oestrogen-active follicles on day 7 than on day 3 (Ireland and Roche, 1983). The dominant follicle of the first wave in cattle may therefore acquire increased responsiveness to LH in response to FSH and thus produce significant quantities of oestradiol (Richards, 1980; Hillier, 1991). There is evidence that in bovine preovulatory follicles, oestradiol exerts positive feedback on its own production (Fortune and Quirk, 1988). Increasing local concentrations of oestradiol within the dominant follicle may in turn further sensitize granulosa cells to FSH, providing a mechanism for continued development in the presence of basal concentrations of FSH (Zelevnik and Hillier, 1984).

The objective of the present study was to assess the importance of FSH during development of the dominant follicle of the first wave of follicular growth during the bovine oestrous cycle. Endogenous secretion of FSH was suppressed using charcoal-

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extracted bovine follicular fluid, a rich source of the glycoprotein inhibin (Robertson *et al.*, 1985), which selectively inhibits secretion of FSH in intact heifers (Quirk and Fortune, 1986; Lussier and Carruthers, 1989; Turzillo and Fortune, 1990). After exposure of dominant follicles to decreased concentrations of basal FSH, luteolysis was induced and the ovulatory capacity of the follicles was assessed and compared with that of controls. We hypothesized that the developing dominant follicle is sensitive to endogenous FSH concentrations, and that depriving this follicle of basal FSH would compromise its ability to continue growing and complete preovulatory maturation. A brief report of the results has appeared in abstract form (Turzillo and Fortune, 1991).

Materials and Methods

Animals

Mature Holstein heifers with normal oestrous cycles were used during the months of January, April and December. Animals were housed in a stanchion barn and fed corn silage and hay with mineral supplement. Oestrous cycles were synchronized by a single injection of 25 mg PGF_{2α} (Lutalyse; Upjohn Co., Kalamazoo, MI) administered i.m. between days 6 and 15 of the cycle. After prostaglandin-induced oestrus, all heifers completed one cycle of normal duration before undergoing further treatment.

Experimental design

Ten heifers were treated at intervals of 12 h with 20 ml charcoal-extracted bovine follicular fluid (bFF) i.v. on days 6 and 7 of the oestrous cycle and six control heifers were treated with 20 ml 0.9% saline following the same schedule. Collection and preparation of the pool of bFF used in these experiments were as described by Turzillo and Fortune (1990). Briefly, bFF was collected at an abattoir and extracted with charcoal to remove steroids. Concentrations of oestradiol and progesterone in the bFF pool were reduced from 63.7 to 0.03 ng ml⁻¹ and from 66.3 to 0.65 ng ml⁻¹, respectively. In a previous study we showed the effectiveness of this pool of bFF in suppressing plasma FSH: injection of 10 ml twice daily completely suppressed the secondary surge of FSH (Turzillo and Fortune, 1990).

On the morning of day 8 (12 h after the final bFF or saline injection) all animals received 25 mg PGF_{2α} i.m. Heifers were observed for oestrous behaviour every 12 h beginning 48 h after PGF_{2α} injection. Blood samples were collected at 4 h intervals from jugular venous catheters (Intracath; 16 g × 12 in, Deseret Medical Inc., Sandy, UT). Sampling began on day 5 and was continued until 16 h after the first observation of oestrus. Catheters were filled with heparin-saline (200 iu ml⁻¹) between sampling times. Blood was centrifuged (2000 g) immediately and plasma was harvested and stored at -20°C for later measurement of FSH, LH, progesterone and oestradiol by radioimmunoassay.

Ovaries were examined daily using a real-time B-mode linear array ultrasound scanner equipped with a 7.5 MHz probe

(Technicare 210DX; Corometrics, North Branford, CT). This procedure has been described in detail by Quirk *et al.* (1986). Heifers were not anaesthetized during ultrasonography. Examinations were recorded on videotape (Ampex Video-cassette, Ampex Corp., Redwood City, CA) and subsequently reviewed on a video monitor (Panasonic NV8950; Matsushita Electric Corp., Secaucus, NJ). Patterns of growth and regression of all follicles with antral diameters ≥ 5 mm were recorded. Ultrasonography was started on day 0 or 1 of the treatment cycle and continued until ovulation occurred, following treatment with PGF_{2α} on day 8 and subsequent oestrus.

Radioimmunoassays

FSH was measured in plasma samples with a homologous radioimmunoassay (Bolt and Rollins, 1983) using USDA-bFSH-B-1 as standard, USDA-FSH-BP3 for radioiodination and antiserum to the bovine FSH-β subunit (USDA-5-0122) as previously reported (Turzillo and Fortune, 1990). Sensitivity of this radioimmunoassay was 0.93 ng per assay tube, with an intra-assay CV of 9.5% and an interassay CV of 15.3%.

Plasma concentrations of LH were measured by heterologous radioimmunoassay (Niswender, 1969) using NIH LH-B9 as standard, ovine LH (LER-1056-C2) for radioiodination and anti-ovine LH (CSU-204) as first antibody. Sensitivity of this assay was 0.07 ng per assay tube. The intra-assay CV was 9.4% and the interassay CV was 15.1%.

Progesterone concentration was determined in plasma samples extracted with petroleum ether (Beal *et al.*, 1980). Recovery of tritiated progesterone added to bovine plasma was 75.5 ± 1.9%. Solvent blanks were negligible and values were not corrected for recovery. Sensitivity of this radioimmunoassay was 12.5 pg per assay tube (0.125 ng ml⁻¹ plasma); intra- and interassay CVs were 9.4% and 9.6%, respectively.

Oestradiol was measured using a modification of a commercially available radioimmunoassay (Second Antibody Estradiol; Diagnostic Products Corp., Los Angeles, CA), validated in our laboratory for measuring oestradiol in bovine plasma extracted with diethyl ether (Turzillo and Fortune, 1990). Recovery of iodinated oestradiol was 88.1 ± 1.0%, and solvent blanks were negligible. Values were not corrected for recovery. Oestradiol concentration in plasma of an ovariectomized heifer (plasma blank) was 0.08 pg per assay tube (0.8 pg ml⁻¹ plasma). Sensitivity of this RIA was 0.07 pg per assay tube (0.7 pg ml⁻¹ plasma), with an intra-assay CV of 14.9% and an interassay CV of 18.9%.

Statistical analyses

Differences in endocrine parameters between control and bFF-treated heifers were assessed by split-plot analysis of variance for repeated measures (SAS, 1985). Student's *t* test was used for comparison of time to oestrus in control versus bFF-treated heifers. For comparison of more than two groups, one-way analysis of variance followed by Scheffé's procedure for separation of means (Lentner and Bishop, 1986) was used to assess differences in time to oestrus following PGF_{2α} and parameters of ovarian follicular growth and regression. All values are presented as means ± SEM.

Table 1. Time to oestrus after injection of heifers with saline or bovine follicular fluid (bFF) twice daily on days 6 and 7 and with PGF_{2α} on day 8 of the oestrous cycle

Treatment	Time to oestrus (days)	Range (days)
Controls (<i>n</i> = 6)	2.6 ± 0.2	2.0–3.5
bFF – all heifers (<i>n</i> = 10)	4.8 ± 0.8*	2.5–8.5
bFF – oestrus not delayed (<i>n</i> = 5)	2.7 ± 0.1	2.5–3.0
bFF – oestrus delayed (<i>n</i> = 5)	6.8 ± 0.6*	5.0–8.5

Values are means ± SEM.

*Significantly different from controls (*P* < 0.05).

Fig. 1. Mean diameters of dominant follicles of the first wave of follicular development in heifers injected i.v. with saline (*n* = 6; —○—) or bovine follicular fluid (bFF) (*n* = 10) twice daily on days 6 and 7 of the oestrous cycle (as indicated by the horizontal bar). Injection of PGF_{2α} on day 8 is indicated by the arrow. Diameters of dominant follicles in animals that exhibited oestrus at the same time as controls (bFF – not delayed; *n* = 5; —▲—) are plotted separately from those in animals that took significantly longer than controls to exhibit oestrus (bFF – delayed; *n* = 5; —■—).

Results

Effects of bFF on time to oestrus

Saline-treated heifers were observed in oestrus 2 or 3 days following injection of PGF_{2α} on day 8 (Table 1); time to oestrus after PGF_{2α} was significantly longer in bFF-treated heifers (*P* < 0.05). Noting the large variability in time to oestrus in animals injected with bFF, we observed two subgroups within the bFF group; five of ten bFF-treated heifers exhibited oestrus at times similar to those in controls, while time to oestrus was significantly longer, compared with controls, in the remaining five bFF-treated animals (*P* < 0.05).

Effects of bFF on follicular dynamics

In response to saline treatment, dominant follicles continued to grow and eventually became ovulatory follicles in all six control animals (Fig. 1). Treatment with bFF differentially

affected dominant follicular development. In bFF-treated heifers in which the time to oestrus following PGF_{2α} injection was not delayed, the dominant follicle of the first wave also became the ovulatory follicle, although its growth was temporarily attenuated during treatment (*P* < 0.05; Fig. 1). Heifers with delayed oestrus did not ovulate the dominant follicle present at the start of bFF injections; no perceptible growth of this follicle occurred during treatment, and it eventually regressed. A second wave of follicular growth appeared in these animals on day 10, and in each case a single follicle was selected to achieve dominance and ovulate (Fig. 2e, f).

No differences were detected between saline- and bFF-treated heifers (regardless of time to oestrus) with respect to day of appearance of the dominant follicle, its growth rate prior to treatment, or its size at the start of treatment (Table 2). As a result of its cessation of growth in response to bFF treatment, the first dominant follicle in bFF-treated animals showing delayed oestrus failed to grow as large as dominant follicles in controls (*P* < 0.05) and reached maximal size earlier than dominant follicles in either control heifers or bFF-treated heifers with no delay to oestrus (*P* < 0.05). Longer persistence (defined as the number of days a follicle was visible with antral diameter ≥ 5 mm) of dominant follicles in bFF-treated animals showing delayed oestrus compared with controls reflects the regression phase of these non-ovulatory follicles. Growth rates of dominant follicles were not different before the start of injections. During treatment, growth of the dominant follicle continued in controls but effectively ceased in bFF-treated heifers (*P* < 0.05). Growth rates of dominant follicles after treatment did not differ between controls and bFF-treated heifers not displaying delayed oestrus.

Regression of the first dominant follicle in bFF-treated animals displaying delayed oestrus was accompanied by recruitment of a second wave of follicular development. The dominant follicle of this wave first appeared on average on day 10.4 ± 0.3, grew 2.1 ± 0.2 mm day⁻¹, reached a maximal diameter of 14.3 ± 1.0 mm on day 14.8 ± 0.7, and persisted for 5.4 ± 0.8 days.

The mean number of follicles with antral diameters ≥ 5 mm comprising the first wave of follicular development did not differ among controls (6.7 ± 1.3 follicles), bFF-treated heifers without delayed oestrus (7.4 ± 1.2 follicles), and bFF-treated heifers displaying delayed oestrus (4.2 ± 0.6 follicles). The mean number of follicles in the second wave of follicular development in heifers with delayed oestrus was 6.6 ± 1.2.

Effects of bFF on endocrine parameters

Mean concentrations of FSH were not different between groups during the 24 h prior to treatment, although a time × treatment interaction was detected during this time (*P* < 0.05). Mean concentrations of FSH in plasma were lower in bFF-treated heifers than in controls during the treatment period (i.e. for 48 h between the first injection on day 6 and the time of PGF_{2α} injection on day 8; *P* < 0.05, Fig. 3). During the 48 h after the end of treatment, FSH concentrations increased but were not significantly higher than values in controls. A time × treatment interaction was detected during this period (*P* < 0.001). When plasma concentrations of FSH in bFF-treated heifers that did not display delayed oestrus were compared with

Fig. 2. Patterns of growth and regression of individual follicles in representative heifers injected with saline or bovine follicular fluid (bFF) during the period indicated by horizontal bars. Arrows denote injection of PGF_{2α} on day 8. Ovulatory follicles are indicated by asterisks. The dominant follicle of the first wave of follicular development ovulated in control heifers (a,b) and in 5 of 10 bFF-treated heifers (c,d). Regression of the first dominant follicle in five bFF-treated heifers was followed by the appearance of a second wave and ovulation of a dominant follicle selected from this wave (e,f).

those in animals in which oestrus was delayed relative to controls, no differences were detected before, during or after the treatment period ($P > 0.05$).

Mean plasma concentrations of LH were not different between saline- and bFF-treated heifers before treatments, during the injection period, or during the 48 h after the end of treatments (data not shown). All animals exhibited a preovulatory surge of LH on the day of oestrus with one exception (discussed below).

Plasma progesterone profiles indicated that a functional corpus luteum was present in all heifers before PGF_{2α} injection, and that complete luteolysis occurred in all cases (Fig. 4a). Mean concentrations of progesterone were similar in bFF- and saline-treated heifers from day 5 to 10 of the oestrous cycle ($P > 0.05$).

Small increases in mean plasma concentrations of oestradiol were observed during the early luteal phase, and small peaks occurred on days 4 and 5 in control and bFF-treated heifers, respectively (Fig. 4b). After injection of PGF_{2α} on day 8, mean concentrations of oestradiol increased and reached maximal

values on day 10 (the day of oestrus) in both control animals and in bFF-treated animals in which oestrus was not delayed. Concentrations of oestradiol in the bFF subgroup exhibiting delayed oestrus remained low until preovulatory increases were observed at about the time of the delayed oestrus (data not shown).

Discussion

Suppression of basal concentrations of plasma FSH was associated with an interruption of growth of the dominant follicle of the first wave in heifers. These results provide support for a critical role of FSH during development of dominant follicles, and suggest that, once selected, the dominant follicle requires normal plasma concentrations of FSH for continued growth and maintenance of functional dominance.

The longer interval between induction of luteolysis and oestrus in some bFF-treated animals in these experiments is similar to results of previous studies in which bFF was

Table 2. Characteristics of the dominant follicle of the first wave of follicular development in heifers treated with saline (controls) or bovine follicular fluid (bFF) on days 6 and 7 and with PGF_{2α} on day 8 of the oestrous cycle

Characteristics of dominant follicle	Controls (n = 6)	bFF – oestrus not delayed (n = 5)	bFF – oestrus delayed (n = 5)
Day of appearance	1.8 ± 0.4 ^a	1.6 ± 0.3 ^a	2.0 ± 0.3 ^a
Size on day 5 (mm)*	11.5 ± 0.7 ^a	11.4 ± 0.5 ^a	11.4 ± 0.5 ^a
Maximal size (mm)*	16.7 ± 0.7 ^a	15.9 ± 0.7 ^{ab}	13.1 ± 0.8 ^b
Day maximal size reached	10.5 ± 0.3 ^a	11.0 ± 0.4 ^a	7.2 ± 1.0 ^b
Persistence (days)	9.7 ± 0.7 ^a	10.6 ± 0.5 ^{ab}	13.6 ± 0.9 ^b
Growth rate before treatment (mm day ⁻¹)**	2.0 ± 0.2 ^a	1.8 ± 0.2 ^a	2.0 ± 0.3 ^a
Growth rate during treatment (mm day ⁻¹)***	0.9 ± 0.2 ^a	0.2 ± 0.1 ^b	-0.1 ± 0.1 ^b

Values are means ± SEM.

^aMeans with no common superscripts within the same row differ significantly ($P < 0.05$).

*Diameter of antrum only.

**Growth rate from day follicle first appeared until day 5.

***Growth rate from day 6 to day 8.

Fig. 3. Concentrations of FSH (means ± SEM) in samples of plasma collected from heifers injected with saline (n = 6; —○—) or bovine follicular fluid (bFF) (n = 10; —▲—) every 12 h during the period indicated by the horizontal bar. The arrow denotes injection of PGF_{2α}. Samples were collected at intervals of 4 h. Data are shown for each treatment until the time when animals began to exhibit preovulatory gonadotrophin surges.

administered during the luteal phase prior to injection of PGF_{2α} (Johnson and Smith, 1985; Wallace and McNeilly, 1985, 1986). Ultrasonography revealed a direct relationship between the fate of the dominant follicle present at the start of treatments and

Fig. 4. Concentrations of (a) progesterone and (b) oestradiol in samples of plasma collected from heifers treated with saline (n = 6; —○—) or bovine follicular fluid (bFF) (n = 10; —▲—) during the period indicated by horizontal bars. Injection of PGF_{2α} is shown by the arrows. In (b), concentrations of oestradiol in bFF-treated animals that exhibited oestrus at the same time as controls (bFF – not delayed; n = 5; —▲—) are plotted separately from those in animals that took significantly longer than controls to exhibit oestrus (bFF – delayed; n = 5; —■—).

the time required for animals to exhibit oestrus. The occurrence of oestrus in control heifers 2 or 3 days after induction of luteolysis, followed by ovulation of the first dominant follicle, confirms previous reports demonstrating the ovulatory capacity of the dominant follicle of the first wave when PGF_{2α} was administered during the growing phase of this follicle (Fortune *et al.*, 1991), on day 7 of the oestrous cycle (Savio *et al.*, 1990), or on day 8 of the oestrous cycle (Kastelic *et al.*, 1990). The longer interval between PGF_{2α} and oestrus in five of ten bFF-treated heifers compared with controls can be explained by regression of the dominant follicle of the first wave and the time required for recruitment of an entire new wave of follicular development. Associated with these events were significantly suppressed concentrations of FSH, which suggests that depriving the dominant follicle of normal basal concentrations of FSH on days 6 and 7 of the oestrous cycle can arrest growth, prevent further developmental changes, and cause a loss of functional dominance, i.e. the ability to suppress development of other follicles.

A surprising finding in this study was the pattern of follicular development in the five bFF-treated heifers that exhibited oestrus at the same time as controls. In a similar way to the dominant follicle of the bFF subgroup that displayed delayed oestrus, the dominant follicle in these heifers stopped growing during the period of suppressed FSH, suggesting that normal

concentrations of FSH are important for growth of the dominant follicle at this stage in its development. The dominant follicles in this group resumed growth and ovulated following luteolysis, despite a similar degree of FSH suppression in these animals as in heifers displaying delayed oestrus. Resumption of growth following temporary follicular arrest has also been observed in women treated with a GnRH antagonist which caused a 50% decline in circulating gonadotrophin concentrations (Kettel *et al.*, 1991). Taken together, these findings indicate that the developing dominant follicle is sensitive to changes in peripheral gonadotrophins, yet can in some cases reinstate normal functions once gonadotrophin support is reinstated.

Because the dominant follicles in all 16 heifers in the study were of similar size before injections were initiated, response patterns cannot be explained by differences in size of the follicle at the time of treatment. One interpretation of these results is that days 6 and 7 may represent a transitional period during development of the dominant follicle of the first wave, when some follicles may be slightly more mature and thus less dependent on FSH support for continued functional dominance. It is possible that the dominant follicles in heifers not displaying delayed oestrus possessed greater sensitivity or responsivity to FSH and were thus capable of completing the final stages of preovulatory maturation. Picton and McNeilly (1991) showed that concentrations of FSH required to stimulate preovulatory follicular development vary markedly among ewes, suggesting that an individual threshold concentration of FSH exists for each animal. This idea is also supported by the observation of marked variations in endogenous concentrations of plasma FSH among ewes (Picton and McNeilly, 1991) and heifers (A. Turzillo, J. Baker and J. Fortune, unpublished observations) within the same breed. Alternatively, it is possible that the duration of decreased FSH concentrations in the present study was insufficient to elicit a completely uniform response in all ten animals injected with bFF.

The consistent suppressive effects of bFF on plasma FSH concentrations confirm previous reports demonstrating the selective influence of inhibin on FSH secretion in cattle (Ireland *et al.*, 1983; Quirk and Fortune, 1986; Beard *et al.*, 1989; Turzillo and Fortune, 1990). The period following bFF injections was characterized in these studies by a rebound in plasma FSH concentrations. In heifers in which the dominant follicle regressed after bFF treatment, the rebound in plasma FSH may have resulted in recruitment of the second follicular wave. We have shown that the secondary FSH surge that occurs about one day after the preovulatory gonadotrophin surges appears to play a role in recruitment of follicles for the first wave (Turzillo and Fortune, 1990), and Adams *et al.* (1992) have demonstrated an association between increases in plasma FSH and the emergence of follicular waves throughout the oestrous cycle in heifers.

There were no significant differences between control and bFF-treated heifers in mean concentrations of LH. However, one heifer in the bFF subgroup in which oestrus was not delayed failed to exhibit a preovulatory surge of LH. This animal exhibited a pattern of follicular characteristics similar to those in the other four heifers in this subgroup, but the dominant follicle of the first wave did not ovulate and became cystic. Although the reasons for the lack of an LH surge in this animal are unknown, they are presumed to be directly related to the ovulatory failure and may not be a direct result of bFF treatment

since this heifer had normal preovulatory concentrations of plasma oestradiol.

Although the administration of bovine inhibin resulted in a consistent and significant suppression of concentrations of peripheral FSH in this study, it must be recognized that the crude preparation of inhibin used also contains numerous other non-steroidal factors (see Ireland, 1987 for review) and potential direct influences of these substances or inhibin itself on follicular growth cannot be clearly dissociated from the effects elicited by changes in plasma FSH. Direct inhibitory effects of ovine (Cahill *et al.*, 1985; Campbell *et al.*, 1991) and bovine (Larson *et al.*, 1991) follicular fluid on growth of follicles in ewes have been reported. However, simultaneous administration of FSH and ovine (McNeilly *et al.*, 1991) or bovine (McNatty *et al.*, 1985; McNeilly, 1985) follicular fluid can prevent the negative effects of follicular fluid on ovarian activity in ewes, and bFF does not inhibit FSH-induced follicular development in prepubertal heifers (Moser *et al.*, 1989a, b). Interpretation of these studies is further complicated by differences in the type of experimental model, dose and purity of FSH preparation, concentration of inhibin (relative to other components) and residual steroid content in follicular fluid used.

In summary, suppression of plasma FSH during the first wave of follicular development in heifers was associated with an interruption of growth of the dominant follicle. When luteolysis was induced at the end of treatment, the dominant follicle in some animals resumed growth and ovulated, but in others the dominant follicle regressed and the ovulatory follicle was selected from a newly recruited wave. These results provide evidence for an important role of FSH during follicular dominance in cattle, and suggest that growth of the dominant follicle of the first wave may require sustained concentrations of FSH.

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