Uterine oxytocin receptors in cyclic and pregnant cows

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Summary. Binding of [³H]oxytocin to uterine subcellular preparations ('oxytocin receptor concentrations') was measured in uterine tissue of heifers and multiparous dairy cows at various stages of the oestrous cycle and during early pregnancy. A method for the assay of ovine uterine oxytocin receptors was optimized for use on bovine tissue. Oxytocin receptor concentrations were increased in cyclic animals around the period of luteolysis and oestrus, rising on Day 15 in endometrium and on Day 17 in myometrium while pregnant animals showed no comparable rise. Receptor concentrations then declined on Day 3 after oestrus in myometrium and on Day 5 in endometrium. Some cyclic animals did not show the expected rise in receptors in the late luteal phase; these animals had abnormally high progesterone concentrations for this stage of the cycle. In animals slaughtered on Day 18 after oestrus and/or insemination which had low oxytocin receptor levels, plasma progesterone concentrations were consistently high; while all animals showing the late luteal phase elevation in receptor values had low progesterone concentrations. Oxytocin receptor and progesterone concentrations were negatively correlated ($P < 0.05$). These data support the hypothesis that oxytocin receptor level is a key factor in the process of luteolysis in cattle and that in pregnancy there is suppression of uterine oxytocin receptor at the expected time of luteolysis. We suggest that uterine oxytocin receptor levels are partly controlled by circulating steroid hormones and are suppressed during early pregnancy.

Keywords: uterus; oxytocin; receptors; cattle; oestrous cycle; pregnancy

Introduction

The secretion of oxytocin and the presence of oxytocin receptors in the uterus is considered important in controlling the episodic patterns of prostaglandin (PG)F-2 α responsible for luteolysis in the ruminant animal (Flint & Sheldrick, 1983; McCracken *et al.*, 1984). Oxytocin receptors have been characterized in the uterus of the rat and sow (Soloff & Swartz, 1974), guinea-pig (Alexandrova & Soloff, 1980), human (Fuchs *et al.*, 1982), sheep (Roberts *et al.*, 1976; Crankshaw *et al.*, 1982; Sheldrick & Flint, 1985) and cow (Schams, 1987; Meyer *et al.*, 1988; Soloff & Fields, 1989). The amount of oxytocin binding to uterine components shows distinct cyclic changes in the ewe, being maximal at the time of luteolysis, then declining in the early luteal phase (Sheldrick & Flint, 1985). This coincides with the time of maximal responsiveness of both myometrium and endometrium to oxytocin stimulation (Roberts *et al.*, 1976). The levels then decline, reaching basal values early in the luteal phase, before which (Day 5) systemically applied oxytocin has a luteolytic effect in the cow (Armstrong & Hansel, 1959; Anderson *et al.*, 1965; Ginther *et al.*, 1967). However, luteal oxytocin concentrations are highest in the early-mid luteal phase, and decline in the late luteal

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phase, reaching a nadir at the time of oestrus (Wathes *et al.*, 1984). This suggests that the PGF-2 α response to peaks of oxytocin at the time of luteolysis is regulated by uterine oxytocin receptor concentrations.

Thus, because uterine oxytocin receptors appear to be the key to the initiation of luteolysis in ruminants, this study investigated the binding of oxytocin to both endometrial and myometrial tissues throughout the cycle and on the relevant days of early pregnancy. The correlation of oxytocin receptor concentration with circulating steroid concentrations was also examined.

Materials and Methods

Animals

Uteri were collected from Holstein $\times$ Hereford and South Devon heifers whose oestrous cycles were synchronized using a single intramuscular injection of 500 mg cloprostenol (Estrumate: Coopers Animal Health Ltd, Crewe, UK). Oestrus, as detected by mounting behaviour, occurred 72–96 h after the administration of cloprostenol. Daily blood samples were taken from the day of synchronization by venepuncture for determination of progesterone profiles. Day 0 was considered to be the day on which progesterone concentrations were at their lowest. In addition, uteri were collected from multiparous cows obtained from the University dairy herd. In this case, cows were monitored by twice-daily observation for signs of behavioural oestrus and collection of daily milk samples for progesterone measurement. Cows were then slaughtered on a specified day of the cycle to allow collection of the reproductive tract. Tissue from cyclic animals was collected on Day 0 (oestrus; N = 9), Day 1 (N = 2), Day 2 (N = 1), Day 3 (N = 2), Day 4 (N = 1), Day 5 (N = 3), Day 6 (N = 2), Day 8 (N = 1), Day 9 (N = 3), Day 12 (N = 3), Day 15 (N = 3), Day 16 (N = 7), Day 17 (N = 3) and Day 18 (N = 10).

For the collection of tissue from pregnant animals, oestrus was similarly induced in heifers and animals were inseminated on the day of oestrus and slaughtered on a specified day of pregnancy. For multiparous cows, insemination occurred on the day of natural oestrus as detected by the herdsman. Plasma samples from heifers and milk samples from cows were collected as described for cyclic animals. The uteri were flushed with 20 ml saline (0.9%: Baxter Health Care, Thetford, Norfolk, UK) within 10 min of slaughter to confirm the presence of an embryo. Animals which had no embryo were described as 'inseminated non-pregnant' (INP). Tissue from pregnant animals was collected on Day 5 (N = 1), Day 7 (N = 2), Day 8 (N = 1), Day 12 (N = 5), Day 13 (N = 3), Day 15 (N = 1), Day 16 (N = 2), Day 18 (N = 9), Day 19 (N = 4), Day 20 (N = 1) and Day 22 (N = 2). Tissue from INP cows was collected on Day 6 (N = 1), Day 7 (N = 1), Day 8 (N = 4), Day 9 (N = 2), Day 10 (N = 1), Day 12 (N = 3), Day 18 (N = 3), Day 19 (N = 6) and Day 20 (N = 2).

Measurement of [3 H]oxytocin binding to uterine preparations

Uteri were collected onto ice immediately after slaughter and dissected in the laboratory within 10 min. Subcellular fractions of endometrium and myometrium were prepared by the method of Sheldrick & Flint (1985). The pellets obtained after ultracentrifugation at 90 000 g were resuspended in 25 mM-Tris-HCl (pH 7.6) using a Polytron homogenizer. This suspension was stored at -196°C until assay. Protein concentrations in the preparations were determined by the method of Lowry *et al.* (1951), using bovine serum albumin standards. To measure oxytocin binding, the method established by Sheldrick & Flint (1985) for sheep preparations was optimized for use with bovine tissue by examining several variables. All optimization investigations were carried out using subcellular fractions prepared from the uteri of cows on the day of oestrus (Day 0).

Time and temperature of incubation. Figure 1(a) shows the effect of time and temperature of incubation on the amount of [3 H]oxytocin bound to the subcellular preparation. From this, an incubation period of 20 min at 20°C was chosen as the optimal time and temperature at which to obtain maximal binding.

Non-specific binding. Increasing concentrations of unlabelled oxytocin were added to the assay tubes to follow displacement of the labelled oxytocin. Concentrations of 0, 1, 10, 100 and 1000 ng oxytocin gave binding values of 770.03 ± 16.3 , 244.30 ± 10.05 , 116.50 ± 10.36 , 93.63 ± 3.78 and 113.93 ± 11.67 fmol oxytocin bound/mg protein, respectively. Thus 100 ng oxytocin was sufficient to cause maximum displacement of labelled oxytocin. Any residual binding (i.e. 116.50 fmol/mg protein) was assumed to be non-specific and not due to the presence of oxytocin receptors. Concentrations below this point were added to the assay to construct a Scatchard plot (Scatchard, 1949) in the presence of 2.5 nM-[3 H]oxytocin. This allowed the determination of a dissociation constant (K_d) value of 1.88 nM.

Addition of cations. In the sheep oxytocin receptor assay, Mn^{2+} ions are added in the form of MnCl_2 to enhance receptor binding. In the bovine assay the addition of MnCl_2 did not enhance binding. However, Mg^{2+} ions did enhance binding, with concentrations of 0, 0.1, 1.0 and 10.0 mM- MgCl_2 in the assay giving binding values of 895.0 ± 2.6 , 1048.0 ± 14.5 , 1101.0 ± 40.3 and 1120.0 ± 105.0 fmol oxytocin bound/mg protein, respectively. Significant increases in binding ($P < 0.001$) were obtained when the concentration of MgCl_2 was increased from 0 to

Fig. 1. Optimization of assay conditions for bovine uterine oxytocin receptors. (a) The effect of time and temperature of incubation on [^3H]oxytocin binding. $\circ$ = 20°C ; $\square$ = 25°C ; $\triangle$ = 30°C . (b) The effect of protein concentration in the sample on the binding of [^3H]oxytocin. (c) A representative Scatchard plot using increasing concentrations of [^3H]oxytocin. (d) Effect of storing tissue at -196°C for 0, 1, 6 or 12 weeks before preparation of subcellular fractions. $\blacksquare$ = pregnant endometrium; $\square$ = pregnant myometrium; $\bullet$ = cyclic endometrium; $\circ$ = cyclic myometrium.

0.1 mM and from 0.1 to 1.0 mM, but not when the concentration was increased further. Therefore, a concentration of 1.0 mM- MgCl_2 was selected as causing optimal binding.

Protein concentration per tube. Because samples contained various concentrations of protein, samples were assayed using different concentrations of membrane protein. Figure 1(b) shows that a linear relationship exists between protein concentration and oxytocin binding. However, all samples were routinely diluted to obtain approximately 50 μg protein per 25 μl before use in the assay to standardize the procedure.

Effect of label concentration on binding of [^3H]oxytocin to receptors. A Scatchard plot was constructed by adding increasing concentrations of labelled oxytocin ([^3H]oxytocin) to the assay (Fig. 1c). This allowed the determination of a K_d of 1.37 nM. Although some scatter is evident, repeated trials have not yielded a closer relationship.

Storage of non-prepared tissue. Tissue was collected from 7 heifers on Day 18 after oestrus (3 cyclic, 3 pregnant and 1 inseminated non-pregnant). One part of each uterus was used immediately for the preparation of subcellular fractions, and the remaining tissue was frozen at -196°C and used 1, 6 and 12 weeks later for the preparation of subcellular fractions. Figure 1(d) shows that there was some variation in the level of oxytocin binding to the preparation over the 12 weeks. Regardless of whether the variation was of a significant level, it was decided that fractions should be prepared immediately after slaughter to minimize any variation caused by storage time.

Modified assay for bovine tissue

For routine assay 50 μg protein were incubated at 20°C for 20 min in 0.1 ml Tris-HCl (25 mM, pH 7.6), containing 0.1% bovine serum albumin (Tris-BSA), 1 mM- MnCl_2 and 2.5 nM-[3,5- ^3H -Tyr]oxytocin (sp. act. 36.6 Ci/mmol; NEN Dupont, Dreierch, West Germany). Non-specific binding was measured in the presence of 100 ng unlabelled oxytocin

(Bachem Ltd, Torrance, CA, USA). Scintillation counting was carried out with an efficiency of 60% (Packard Instruments model 1900CA). Inter- and intra-assay coefficients of variation for measurement of receptor concentrations were 16.0% and 9.3% respectively. The sensitivity of the assay was 69.5 fmol/mg protein, and 50% displacement of tracer occurred between 0.5 and 1.0 pmol/tube. Binding of [^3H]oxytocin to the filters (GVWP filters, pore size 0.22 μm , Millipore, Watford, Herts, UK) in the absence of uterine extract was 0.18%. Oxytocin binding was expressed as fmol oxytocin bound/mg protein. K_d values obtained from the receptor were 1.37 nM when calculated by adding increasing concentrations of [^3H]oxytocin to the assay, and 1.88 nM when calculated by displacement of [^3H]oxytocin by increasing concentrations of unlabelled oxytocin.

Radioimmunoassay of progesterone

Progesterone was measured in duplicate 100 μl plasma samples as described by Haresign *et al.* (1975) and modified by Hunter *et al.* (1986). Samples were randomized throughout each assay. The inter- and intra-assay coefficients of variation were <15% and <10% respectively. The limit of sensitivity was 0.23 ng/ml. Milk progesterone concentrations were determined as described by Gadsby *et al.* (1974) and modified by Bulman & Lamming (1978). Inter- and intra-assay coefficients of variation were <20% and 9% respectively, and the limit of sensitivity was 2 ng/ml.

Statistical analysis

The results were analysed using GENSTAT on the University of Nottingham VME computer. Oxytocin receptor profiles were analysed by a linear regression of oxytocin receptors upon Day combined with the progesterone concentrations on the day of slaughter. This was followed by an analysis of variance across day of cycle or pregnancy and reproductive status. Differences between cyclic, pregnant and inseminated non-pregnant animals on Days 12 and 18 were tested by Student's *t* test.

Results

Binding of [^3H]oxytocin to uterine membranes ('oxytocin receptor concentration') measured in cyclic cows is shown in Fig. 2(a) while Fig. 2(b) shows the data collected from pregnant cows. Concentrations were significantly higher at the time of luteolysis in cyclic cows than at the corresponding time in pregnant cows ($P < 0.05$). Figure 2(c) shows the data collected from inseminated non-pregnant cows. Data for all cyclic cows which had abnormally high progesterone concentrations for the late luteal phase, and did not show high receptor levels at this time are shown in Fig. 2(d).

In cyclic animals oxytocin binding in endometrial tissues began to rise at Day 15 after oestrus, while myometrial binding did not begin to rise until Day 17. Binding in both tissues then remained high until Day 3 after oestrus in myometrium and Day 5 in endometrium.

The regression of oxytocin receptor concentrations in the endometrium upon day showed a quadratic relationship with the nadir occurring on Day 9 ($P < 0.05$; Fig. 2a). When plasma progesterone concentrations were combined with the effect of day, a significantly greater proportion of the variance in these receptor data was accounted for ($P < 0.05$) such that progesterone concentrations were negatively correlated with oxytocin receptor concentrations.

On Day 18 after oestrus there was a distinct difference between pregnant and cyclic animals in terms of both oxytocin receptor binding and progesterone concentrations although, again, some of the non-pregnant animals showed abnormal progesterone concentrations and corresponding low levels of oxytocin receptors (Table 1).

Discussion

These results show that uterine oxytocin binding through the bovine oestrous cycle follows a pattern similar to that reported for the sheep (Sheldrick & Flint, 1985), with endometrial levels generally exceeding those in myometrial tissue (Roberts *et al.*, 1976; Sheldrick & Flint, 1985) and highest at luteolysis, coinciding with the withdrawal of progesterone from the circulation. This is consistent with the hypothesis proposed by Vallet *et al.* (1990) that receptor levels are influenced by

Fig. 2. Oxytocin receptor concentrations (a) through the oestrous cycle, (b) in early pregnant cows, (c) in inseminated non-pregnant cows and (d) in cyclic cows showing abnormal progesterone concentrations at slaughter. ○ = endometrium; ● = myometrium. In (a) the regression lines are fitted by 4th order regressions (Sigma Plot 4 Scientific Graph System, Jandel Scientific, CA, USA).

Table 1. Mean $\pm$ s.e.m. oxytocin receptor concentrations (fmol/mg protein) in endometrial and myometrial tissue, and plasma progesterone concentrations on Day 18, in cyclic and pregnant cows, and in cyclic cows which still have high plasma progesterone concentrations

	Cyclic	Pregnant	High progesterone†
Oxytocin receptors			
Endometrium	563.4 $\pm$ 117	18.1 $\pm$ 4.6*	52.3 $\pm$ 23.4*
Myometrium	82.3 $\pm$ 9.8	75.3 $\pm$ 7.7	71.9 $\pm$ 13.8
Progesterone (ng/ml)	0.93 $\pm$ 0.4	8.37 $\pm$ 0.7*	10.5 $\pm$ 1.1*
No. of cows	4	6	4

*Significantly different from cyclic animals ($P < 0.05$).

†Of these 4 animals, 3 were inseminated non-pregnant. The cyclic animal had values of 45.9, 97.4 and 9.5 for endometrial and myometrial oxytocin receptors and progesterone concentrations, respectively.

circulating steroid concentrations, being initially suppressed and later stimulated by progesterone. The subsequent rise in uterine oxytocin receptor concentrations therefore causes luteolysis, thus bringing about the eventual decline in luteal progesterone production. It has been postulated that luteal phase progesterone inhibits receptor formation (Soloff, 1975; Nissenson *et al.*, 1978; Sheldrick & Flint, 1985). However, the precise interaction between ovarian steroid hormones and the presence of uterine oxytocin receptors remains to be defined. The present study confirms that cows with uncharacteristically low oxytocin receptor levels for the late luteal phase have correspondingly high plasma progesterone values. McCracken *et al.* (1984) showed that oestradiol induces oxytocin receptor formation in ewes, while the results of Parkinson *et al.* (1990) also show a positive correlation between plasma oestradiol concentrations and uterine oxytocin receptor levels, along with a negative correlation between plasma progesterone and uterine oxytocin receptor concentrations. One possible explanation could be that oxytocin receptor formation is influenced by the preovulatory oestradiol rise, and the interaction of oxytocin with the uterine receptors induces PGF-2 α release and brings about luteolysis and thus a decline in progesterone concentrations. The alternative preferred explanation is that progesterone eventually loses its inhibitory effect on uterine oxytocin receptors.

There appears to be a slight rise in oxytocin receptor values in the myometrium on Day 12 after oestrus in pregnant and inseminated non-pregnant cows compared to cyclic cows in which mean oxytocin binding on Day 12 is below the limit of sensitivity of the assay. A small but significant depression of progesterone concentrations occurs in mated but subsequently non-pregnant cows on Day 12 after mating (Lamming *et al.*, 1989). The small change in ratio of progesterone to oestradiol concentrations in such animals may be sufficient to allow the development of myometrial oxytocin receptors, and be responsible for the small episodes of PGF-2 α release shown in pregnant and non-pregnant cows about 12 days after ovulation (Parkinson & Lamming, 1990).

Administration of oxytocin early in the cycle brings about luteolysis in cattle (Armstrong & Hansel, 1959; Anderson *et al.*, 1965; Ginther *et al.*, 1967), which can be prevented by hysterectomy (Armstrong & Hansel, 1959). Such infusions of oxytocin on Days 2 and 3 of the cycle cause increased peripheral PGFM concentrations (Oyedipe *et al.* 1984), and oxytocin administration at this time therefore causes premature luteolysis by stimulating PGF-2 α production. The present results confirm that this occurs due to the continued presence of elevated amounts of oxytocin receptor in the myometrium until Day 3 and in the endometrium until Day 5 of the new cycle. Furthermore, these results on the temporal changes in uterine oxytocin receptor levels probably explain previous reports of the effects of oxytocin infusion in the mid-late luteal phase on PGFM levels and cycle length extension in cows. Kotwica *et al.* (1988) showed that infusion of oxytocin

beginning on Day 14, 15 or 16 in cyclic animals resulted in a plasma PGFM response and no extension of cycle length, whereas Gilbert *et al.* (1989) infused oxytocin from Day 10 after oestrus and obtained no PGFM response and a significant extension of cycle length. This would suggest that the bovine uterus becomes susceptible to oxytocin between Day 10 and Day 14 of the cycle, the presence of oxytocin before this time possibly causes a down-regulation of the oxytocin receptor (Flint & Sheldrick, 1985), and this could explain the results of Lamming *et al.* (1989).

Luteolysis in the non-pregnant animal is caused by the episodic release of PGF-2 α from the uterus in a positive feedback loop involving oxytocin release from the corpus luteum (Flint & Sheldrick, 1983), although the process by which this loop is initiated is not yet clear. Circulating oxytocin concentrations in bovine plasma are highest in the mid-luteal phase (Schams *et al.*, 1985), corresponding to the oxytocin content of the corpus luteum at this time. In the cow a decline in luteal oxytocin concentration precedes luteolysis (Wathes *et al.*, 1984), which suggests that the response to oxytocin during the process of luteolysis is regulated by oxytocin receptor levels, rather than by circulating oxytocin concentrations. This suggestion is supported by the fact that changes in oxytocin receptor levels in endometrium and myometrium correlate well with alterations in the responsiveness of these tissues to oxytocin stimulation. Maximal responsiveness of the endometrium to oxytocin in terms of PGF-2 α secretion occurs on Day 15 in cyclic ewes (Roberts *et al.*, 1976), while the maximum luteolytic effect of oxytocin in cows occurs early in the cycle (up to Day 5; Armstrong & Hansel, 1959) and at the end of the cycle (Day 15 onwards; McCracken *et al.*, 1984) when receptor concentrations are at their highest.

Table 2. Dissociation constants (K_d , nM) for uterine oxytocin receptors reported in the literature for sheep and cows

Species	Authors	Endometrium	Myometrium
Sheep	Roberts <i>et al.</i> (1976)	(range 0.5–0.7)	
	Crankshaw <i>et al.</i> (1982)	—	1.8 $\pm$ 0.2
	Pliska <i>et al.</i> (1984)	—	1.0, 50, > 10 ⁻⁴
	Sheldrick & Flint (1985)	(a) 1.96	2.19
		(b) 1.87	
Cattle	Kotwica <i>et al.</i> (1988)	(c) 1.74	
		(d) 1.30	
		1.83 $\pm$ 0.59	—
		14.9 $\pm$ 3.2	1.2 $\pm$ 0.16
	Soloff & Fields (1989)	(range 1.3–25.7)	
		(e) 1.37	—
	Present study	(f) 1.88	

(a) Measured in caruncular tissue; (b) measured in inter-caruncular tissue; (c) measured in tissue taken on Day 21 of the oestrous cycle; (d) measured in tissue taken on Day 1 of the cycle; (e) measured by increasing [³H]-oxytocin concentration; (f) measured by increasing unlabelled oxytocin concentration.

The oxytocin content of the ovine corpus luteum and, consequently, circulating concentrations of oxytocin decline in early pregnancy (Sheldrick & Flint, 1983). This has been suggested to be one way in which the endocrine environment of the mother is adapted to pregnancy (Sheldrick & Flint, 1983; Schams & Lahlou-Kassi, 1984). A similar reduction in the concentration of the oxytocin prohormone mRNA occurs at the same time in sheep (Jones & Flint, 1988) and in cows (Ivell *et al.*, 1985). Oxytocin receptor levels in pregnant ewes are low at the expected time of luteolysis (Sheldrick & Flint, 1985), and the present study has demonstrated that this also occurs in the cow. It has been suggested that maintaining oxytocin receptors at a low level in pregnancy may be a way in which uterine responsiveness to oxytocin is reduced, in order to ensure a decreased uterine secretion of PGF-2 α at this time (Sheldrick & Flint, 1985; Flint & Sheldrick, 1986), and hence the maintenance of high progesterone levels necessary for pregnancy. The process by which luteolysis is

blocked depends upon the presence of an embryo and its production of a trophoblastic interferon (tIFN) (Godkin *et al.*, 1984; Vallet *et al.*, 1988). However, the mechanism by which oxytocin receptor levels are prevented from rising by tIFN is uncertain. In sheep it is possible that this antiluteolytic effect depends upon blastocyst production of tIFN shown to be an $\alpha 2$ -interferon (Stewart *et al.*, 1987; Imawaka *et al.*, 1987), the properties of which are under investigation (Stewart *et al.*, 1989). The presence of a similar trophoblastic protein, bTP-1, is being investigated in cows (Bazer *et al.*, 1986; Godkin *et al.*, 1988; Helmer *et al.*, 1989). Another possibility is blastocyst production of oxytocin, which may down-regulate receptor levels in a manner similar to that observed following continuous oxytocin administration to ewes (Flint & Sheldrick, 1985; Sheldrick & Flint, 1987). There is conflicting evidence as to whether the ovine conceptus contains or secretes oxytocin (see Flint *et al.*, 1989) or that intrauterine infusion of oxytocin blocks oxytocin receptor formation (unpublished data). However, systemic infusion of oxytocin can block luteolysis in cows if administered beginning on Day 10 (Gilbert *et al.*, 1989).

From previous reports in cows and ewes it appears to have been consistently difficult to calculate precise dissociation constants for the receptor (see Table 2). Pliska *et al.* (1984) reported multiple binding sites in ovine myometrium while Soloff & Fields (1989) failed to obtain a consistent Scatchard plot for bovine endometrium, and have published a range of values for K_d . Kotwica *et al.* (1988) published different values for K_d depending on the stage of the cycle, suggesting that the affinity of the receptor changes through the cycle. Meyer *et al.* (1988) reported a K_d value for bovine endometrium which is very similar to the values found here, and showed that [3 H]oxytocin binding to the endometrium occurs from Day 17 to Day 6, and is maximal on the day of oestrus.

In conclusion the close correlation between progesterone and endometrial oxytocin receptor concentrations illustrates that the rise in endometrial oxytocin receptor levels is likely to be important in the initiation of luteolysis. This therefore adds evidence to the hypothesis that uterine oxytocin receptor concentrations are important in the process of luteolysis in the cow, and the prevention of the uterine rise in uterine oxytocin receptors is important in the maternal recognition of pregnancy and the maintenance of pregnancy. In the cyclic cow oxytocin receptor levels are closely correlated to the steroid environment, a situation modified in the pregnant animal by the appearance and activity of tIFN.

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