Relationship between ovulation rate and concentrations of insulin-like growth factor-1 in plasma during the oestrous cycle in various genotypes of sheep

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To determine whether concentrations of insulin-like growth factor-1 (IGF-1) in blood of ewes change during the oestrous cycle, oestrus was synchronized for 45 ewe lambs from four genotypes (Finn ewes selected for low ovulation rate (LF), Finn ewes selected for high ovulation rate (HF), unselected control Finn ewes (CF) and Cambridge ewes (CAM)) using progestin sponges and blood samples were taken every day from day 0 (day 0 = day of progestin sponge removal) to day 5, and then every second or third day until 3 days after the next oestrus. Ovulation rates (determined via laparoscopy) following the first oestrus were 1.3, 3.3, 2.0 and 2.1 for LF, HF, CF and CAM groups, respectively. In a second experiment, jugular and utero-ovarian venous blood samples were collected simultaneously from seven Booroola crossbred ewes during the mid-luteal phase of an oestrous cycle to determine whether the ovary is a major source of blood IGF-1. In the first experiment, plasma IGF-1 concentrations increased ($P < 0.05$) between days 0 and 3, and then decreased ($P < 0.05$) between days 4 and 8 in all groups. IGF-1 concentrations increased again at the subsequent oestrus. There was no significant difference in plasma IGF-1 between HF and LF ewe lambs. Overall, plasma IGF-1 was lowest ($P < 0.05$) in CAM and highest in CF ewe lambs at all stages. Plasma IGF-1-binding protein activity did not vary with stage of cycle or differ ($P > 0.10$) among genotypes. Among LF, HF and CF ewe lambs, ovulation rate was not correlated with plasma IGF-1 or IGF-1-binding protein activity. In the second experiment, serum concentrations of IGF-1 in jugular (174 ± 38 ng ml$^{-1}$) and utero-ovarian (188 ± 43 ng ml$^{-1}$) venous blood did not differ ($P > 0.10$) but were highly correlated ($r = 0.96$). We conclude that (i) plasma concentrations of IGF-1 increase during oestrus in cyclic ewes, (ii) plasma concentrations of IGF-1 are influenced by genotype in sheep but are not genetically associated with ovulation rate, (iii) plasma IGF-1-binding protein activity is not influenced by stage of cycle or genotype in sheep, and (iv) the ovary does not appear to be a major source of blood IGF-1.

Introduction

Ovulation rate in sheep can be altered by genetic selection and by changes in a wide range of environmental factors. The effects of such manipulations are mediated via a complex endocrine control of ovarian follicular development and function. In Booroola and Romanov ewes (ovulation rate of 3 to 5), concentrations of FSH in the pituitary and in plasma are significantly higher than in control ewes (ovulation rate of 1 or 2) during various periods of the oestrous cycle (Cahill et al., 1981; Robertson et al., 1984; McNatty et al., 1987). Evidence suggests that reduced ovarian inhibin production may be at least partially responsible for the increased FSH secretion observed, because inhibin content of ovaries in Booroola ewes with a copy of the Fecundity (F) gene is significantly lower than in ewes without the F gene (Cummins et al., 1983). However, differences in FSH secretion among other high fecundity breeds of sheep have not been observed. FSH secretion in Finn ewes (ovulation rate of 2 to 4) and less prolific ewes (ovulation rate of 1 or 2; e.g. Suffolk: Webb and England, 1984; Wheaton et al., 1988; Galway: Admas et al., 1988) do not differ. Thus, factors other than inhibin or FSH production must be invoked as regulators of ovulation rate.

We have reported that cows selected for twinning have significantly higher concentrations of insulin-like growth factor-1 (IGF-1) in serum and follicular fluid than do control cows (Echtternkamp et al., 1990). IGF-1 has also been shown to have dramatic stimulatory effects on proliferation and steroidogenesis.

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of cultured granulosa and thecal cells (Geisthovel et al., 1990; Hammond et al., 1991). In addition, the concentration of IGF-1 in the peripheral circulation appears to be genetically determined in several mammalian species (Merimee et al., 1982; Buonomo et al., 1987; Blair et al., 1988). IGF-1 may, therefore, be a potential endocrine regulator of ovulation rate in sheep. The objective of the present investigation was to determine whether the differences in ovulation rate between low and high ovulation rate lines of Finn sheep, developed by selection from the same base population, are associated with differences in plasma IGF-1 concentrations. The present study also included Cambridge sheep which have a high ovulation rate, which is thought to be due to a major gene (Hanrahan, 1991). In addition, serum IGF-1 was measured in jugular and utero-ovarian venous blood of ewes to determine whether the ovary is a major source of IGF-1 in blood.

Materials and Methods

Experiment 1

Ewe lambs from four genetic lines were used in Expt 1: Finn lines selected for low ovulation rate (LF; n = 11), high ovulation rate (HF; n = 10) or unselected control line (CF; n = 13), and the Cambridge breed (CAM; n = 16). All ewe lambs were housed under natural photoperiod at the Western Research Centre and offered grass silage ad libitum supplemented with a concentrate pellet (350 g per head per day). All ewe lambs were approximately 9 months of age (nulliparous) at the start of the study and were all the available ewe lambs born in 1990 in these lines.

Oestrous cycles of ewe lambs were synchronized by insertion of progesterin (60 mg medroxyprogesterone acetate) sponges for 11 days in January, 1991. Starting on the day of sponge removal (day 0), ewe lambs were bled via jugular venepuncture every day (between 10:30 and 12:30 h) to day 6, and then every second or third day until 3 days after the next oestrus. Plasma was harvested and frozen at −20°C until analysed for IGF-1. All ewe lambs except three in the CAM group had commenced ovarian cyclicity in November (approximately 7 months of age) and exhibited oestrous cycles before sponge insertion. Ovulation rate (i.e. number of corpora lutea) was assessed by laparoscopy on day 9 after sponge removal. All ewe lambs undergoing laparoscopies were given a local anaesthetic (2% lignocaine) at the sites of trocar insertion on the abdominal wall. Ewe lambs were not fasted prior to the laparoscopy on day 9. Vasectomized rams were used to check the ewe lambs for the onset of oestrus following sponge removal (twice a day) and once a day for onset of the second oestrus following sponge removal. Body weights were recorded on day 8 following sponge removal.

Experiment 2

To determine whether the ovary is a major source of plasma IGF-1, Rambouillet crossbred ewes (n = 7) were maintained in a common flock at El Reno on grass pasture until 4 weeks before blood collection. During the 4 weeks immediately before blood collection, the ewes were supplemented with corn (0.45 kg per head per day) and medium quality grass hay ad libitum. Jugular and utero–ovarian blood samples were collected simultaneously during the mid-luteal phase of an oestrous cycle. All ewes undergoing surgery (midline incision) were anaesthetized with a combination of xylazine (0.22 mg kg⁻¹ i.m.) and ketamine (11 mg kg⁻¹ i.m.). Utero–ovarian venous blood was collected with needle and syringe approximately 2 to 3 cm posterior to the bifurcation of the ovarian and uterine branches of the utero–ovarian vein. Serum was collected and stored as described in Expt 1.

IGF-1 radioimmunoassay

Plasma/serum samples were stored at −20°C until concentrations of IGF-1 were determined by radioimmunoassay after acid–ethanol extraction as described previously (Echternkamp et al., 1990; Spicer and Zavy, 1992). The intra- and interassay coefficients of variation were 8.9 and 17.0%, respectively. Briefly, aliquots of plasma/serum were diluted 1:4 with 87.5% acidic ethanol (0.25 mol HCl 1⁻¹ final concentration) and incubated for 16 h at 4°C. Samples were then centrifuged for 30 min at 1200 g at 4°C and neutralized with 0.855 mol Tris 1⁻¹. This procedure resulted in parallelism between the human IGF-1 standard (R&D Systems, Minneapolis, MN) and ovine plasma using an IGF-1 antiserum (UB3-189) provided by the National Hormone and Pituitary Program (Baltimore, MD) (see Fig. 1). Addition of 2.5 ng of recombinant human IGF-2 (R&D Systems, Minneapolis, MN) per tube did not affect parallelism between ovine plasma and the IGF-1 standard (Fig. 1). Crossreactivity with human IGF-2 and bovine insulin was ≤ 0.2% and < 0.001%, respectively.

Fig. 1. Competition of acid–ethanol treated ovine plasma with (○—○) or without (□—□) 2.5 ng of IGF-2 added per tube in the IGF-1 radioimmunoassay. A pool of plasma collected from 12 ewe lambs (three ewe lambs from each genotype) was treated as described in Materials and Methods. Increasing volumes of diluted extract are expressed in µl plasma equivalents added per tube as percentage of total binding (Buffer control) of 125I-labelled IGF-1 on a log–logit plot. Displacement curve for authentic IGF-1 (●—●) is also shown.
IGF-1-binding protein activity

IGF-1-binding protein activity in plasma/serum was determined by incubation with $^{125}$I-labelled IGF-1 as previously described (Moses et al., 1979; Spicer et al., 1992a). Intra- and interassay coefficients of variation were 5.2 and 9.2%, respectively.

Statistical analysis

For Expt 1, plasma IGF-1 and IGF-1-binding protein data were subjected to split-plot analysis of variance (ANOVA) with ewe lambs nested within genotype and day after sponge removal as the subplot. Body weight and ovulation rate data were analysed by one-way ANOVA. Differences among genetic groups were evaluated using a priori orthogonal contrasts among the Finn lines (HF versus LF and CF versus mean of LF and HF) while CAM was compared with CF. Differences due to day were assessed using Fisher’s Protected (i.e. only if F test was significant) least significant difference mean test (Ott, 1977). In addition to an overall analysis, the data were used to form three subsets corresponding to samples for days 1 to 5, 6 to 16, and 17 to 21 following sponge removal to provide an assessment of line differences at follicular and luteal phases of the oestrous cycle, and to evaluate the reproducibility of differences among ewe lambs within lines at each of these stages. Five (including the three ewe lambs that had not yet exhibited oestrus or ovulated before sponge insertion) of 16 CAM ewe lambs did not exhibit oestrus or ovulate after sponge removal and consequently data from these animals were excluded from all analyses. For Expt 2, jugular and utero-ovarian IGF-1 concentrations and IGF-1-binding protein activity were compared by Student’s paired t test.

Results

Experiment 1

Body weights were significantly different among genotypes (Table 1); LF ewes weighed less ($P < 0.05$) than CF and CAM ewes. Body weight of HF ewes did not differ ($P > 0.10$) from LF, CF or CAM ewes. Ovulation rate (Table 1) was greater ($P < 0.05$) in CF and CAM ewes than in LF ewes. The ovulation rate in HF ewes was greater ($P < 0.05$) than in CF, CAM and LF ewes (Table 1). Ovulation rate was not correlated with body weight among LF, CF and HF ewes ($r = 0.22, P > 0.10; n = 34$) or within CAM ewes ($r = 0.22, P > 0.10; n = 11$).

The Finn lines did not differ with respect to the timing of oestrus following sponge removal or cycle length (Table 1). However, the interval from sponge removal to first oestrus was significantly longer ($0.67 \pm 0.19$ days) for CAM ewes versus the mean of the Finn lines; the mean intervals from sponge removal to onset of first oestrus were $2.1, 2.1, 1.9$ and $2.7$ days (SEM = 0.14) for LF, CF, HF and CAM ewes, respectively.

Concentrations of IGF-1 in plasma were affected by stage of the oestrous cycle ($P < 0.001$). Plasma concentrations of IGF-1 increased ($P < 0.05$) between days 0 and 4 after sponge removal and then decreased ($P < 0.05$) between days 4 and 8 in all groups of ewes (Fig. 2). Concentrations of IGF-1 increased sooner ($P < 0.05$) after sponge removal in LF, CF and HF ewes than in CAM ewes (Fig. 2). There were significant differences among genetic groups at all stages of the oestrous cycle, and although the source of these differences varied with stage of the cycle, there was no significant difference between HF and LF lines at any stage, although the difference approached significance ($P < 0.08$) during the luteal phase (days 8 to 16 after sponge removal). Concentrations of IGF-1 were higher for the CF line compared with the mean of the two selected lines at all stages ($P < 0.05$). IGF-1 concentrations were lower in CAM ewes than in CF ewes throughout the sampling period but this difference was significant only during the follicular phases (days 1 to 5 and days 18 to 21 after sponge removal); the difference between CF and CAM ewes approached significance ($P < 0.08$) during the luteal phase (days 8 to 16). Averaged across all days, the mean values (SEM) were $134 \pm 20, 170 \pm 18, 217 \pm 17$ and $134 \pm 19$ ng ml$^{-1}$ for HF, LF, CF and CAM ewes, respectively. Average concentrations of IGF-1 in plasma were correlated with body weight among HF, CF and LF ewes ($r = 0.64, P < 0.05$) but not correlated in CAM ewes ($r = 0.17, P > 0.10$). Ovulation rate did not significantly correlate ($P > 0.10$) with plasma concentrations of IGF-1 in any genotype of ewe.

The variability of IGF-1 concentrations among ewes was relatively high (CV about 45%) and differences among ewes were highly reproducible from day to day. Thus, the reproducibility of concentrations of plasma IGF-1, pooled across lines, among days 1 to 5, days 8 to 16 and days 18 to 21 were 0.72, 0.82 and 0.74, respectively.

Plasma IGF-1-binding protein activity was measured on days 3 and 14 after sponge removal and did not differ ($P > 0.10$) between genotypes or between days 3 and 14 (Table 2). Within LF, CF, HF and CAM ewes, plasma IGF-1-binding protein activity did not correlate with plasma IGF-1 within day ($r = -0.18, -0.34, 0.07$ and $0.24$, respectively; $P > 0.10$) or day $14$ ($r = 0.38, 0.25, 0.59$ and $-0.11$, respectively; $P > 0.07$). There was no significant correlation between average plasma IGF-1-binding protein activity and either ovulation rate or body weight.

Experiment 2

Concentrations of serum IGF-1 did not differ ($P > 0.10$) between jugular ($174 \pm 38$ ng ml$^{-1}$) and utero-ovarian ($188 \pm 43$ ng ml$^{-1}$) venous blood. In addition, concentrations of IGF-1

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of ewes</th>
<th>Ovulation rate*</th>
<th>Cycle length (days)</th>
<th>Body weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF</td>
<td>10</td>
<td>3.3*</td>
<td>17-0</td>
<td>33.8*</td>
</tr>
<tr>
<td>LF</td>
<td>11</td>
<td>1.3*</td>
<td>17-3</td>
<td>31.0*</td>
</tr>
<tr>
<td>CF</td>
<td>13</td>
<td>2.0*</td>
<td>17-1</td>
<td>35.1*</td>
</tr>
<tr>
<td>CAM</td>
<td>11</td>
<td>2.1*</td>
<td>17-4</td>
<td>36.6*</td>
</tr>
<tr>
<td>SEM</td>
<td>0.2</td>
<td>0.3</td>
<td>1.1</td>
<td></td>
</tr>
</tbody>
</table>

*Ovulation rate 9 days after removal of progestin sponge.

ab: Within-column values with different superscripts are significantly different ($P < 0.05$).
Table 2. Least squares means of IGF-1-binding protein activity in plasma of Finn ewe lambs selected for high ovulation rate (HF), low ovulation rate (LF) and unselected control Finn ewe lambs (CF), and Cambridge (CAM) ewe lambs in Expt 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of ewes</th>
<th>Day after sponge removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>LF</td>
<td>7.3</td>
<td>14</td>
</tr>
<tr>
<td>CF</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>CAM</td>
<td>11</td>
<td>14</td>
</tr>
</tbody>
</table>

*IGF-1-binding protein activity is expressed as percentage of 125I-IGF-1 specifically bound per 10 µl plasma.

in jugular and utero-ovarian venous blood were positively correlated \((r = 0.96, P < 0.01)\). Serum IGF-1-binding protein activity also did not differ \((P > 0.10)\) between jugular \((7.72 \pm 0.36\% \text{ per } 10 \mu l)\) and utero-ovarian \((7.75 \pm 0.34\% \text{ per } 10 \mu l)\) venous blood. Serum IGF-1-binding protein activity in jugular and utero-ovarian venous blood was also positively correlated \((r = 0.72, P < 0.05)\).

**Discussion**

We have reported that ovariectomy causes a decrease in serum IGF-1 in cattle (Richards et al., 1991; Spicer et al., 1992b), and that exogenous oestradiol causes a significant increase in serum IGF-1 concentrations in ovariectomized cows (Richards et al., 1991). Furthermore, ovarian concentrations of IGF-1 in rats are greatest during oestrus (Carlsson et al., 1989). The consistent and large increase in plasma IGF-1 observed in the present study shortly after sponge withdrawal, reaching a maximum about one day after the onset of oestrus, suggests that follicular oestrogens may regulate IGF-1 secretion in sheep as suggested for cattle. In further support of this interpretation, the five ewes that did not exhibit oestrus or ovulate following sponge removal did not have any increases in plasma IGF-1 (data not shown).

The absence of a significant difference in IGF-1 concentrations between the divergently selected Finn lines together with the fact that IGF-1 concentrations in the control line were significantly higher than both selected lines, throughout the oestrous cycle, leads to the rejection of the hypothesis that IGF-1 is a key endocrine determinant of genetic differences in ovulation rate in sheep. This conclusion is consistent with results from a preliminary study of 20-month-old ewes from these three lines of Finn sheep which showed that plasma IGF-1 concentrations on the day of oestrus or during the luteal phase of the cycle were not associated with differences in ovulation rate (Spicer et al., 1991c). Driancourt et al. (1990) observed that ewes from the HF lines recruited more follicles, which produced smaller preovulatory follicles, each containing a smaller number of granulosa cells compared with either the low- or control-line ewes. Moreover, the atresia rate of follicles larger than 0.7 mm did not differ among groups of Finn ewes formed on the basis of high or low ovulation rate (Banoin et al., 1991). Thus, smaller follicles with fewer granulosa cells in the high-line Finn ewes may be due, in part, to lower concentrations of IGF-1 in plasma (which would presumably be a smaller mitotic stimulus to granulosa cells). A recent study has shown that oestradiol...
production per granulosa cell as well as testosterone production per thecal cell were significantly greater in Finn ewes selected for high ovulation rate versus Finn ewes selected for low ovulation rate (Driancourt and Hanrahan, 1991), suggesting that differences in plasma IGF-1 may also be involved in regulating genotypic differences in follicular steroidogenesis. However, these Finn lines do not differ in their hypothalamic/pituitary sensitivity to oestradiol negative feedback (Webb et al., 1992).

Cambridge ewes show an exceptionally high variability and repeatability of ovulation rate which is attributed to segregation of a gene with a large effect on ovulation rate (Hanrahan, 1991). Plasma concentrations of IGF-1 in CAM ewe lambs were significantly lower than in CF ewe lambs and had similar ovulation rates, and no positive correlation was evident between plasma IGF-1 concentrations and ovulation rate within CAM or Finn lines (present study). These observations again support the conclusion that there is no causal connection between plasma IGF-1 and genetic differences in ovulation rate. In contrast, we have observed that concentrations of IGF-1 in serum are significantly greater (by 32%) in 18-month-old prolific Finn × Rambouillet ewes (ovulation rate = 1.88) than in less prolific Dorset × Rambouillet ewes (ovulation rate = 1.35) (Spicer and Zavy, 1992). However, this apparent association between ovulation rate and IGF-1 concentration was not observed in older (30 month-old) ewes of the same genotypes (Spicer and Zavy, 1992). Further studies will be required to establish whether and how IGF-1 affects follicular growth and ovulation rate in only certain genotypes of ewes at certain ages. Nevertheless, the high repeatability of plasma IGF-1 in sheep may imply that genetic differences are due to a few genes with relatively large effects. Other hypotheses that have been proposed to explain increased ovulation rates in various breeds of sheep include (i) greater number of large antral follicles with lower atretic rates (Lahlo-Kassi and Mariana, 1984); (ii) prolonged recruitment and low intensity of selection of follicles destined to ovulate (Driancourt et al., 1985); (iii) a need for more follicles to produce the same quantity of oestriadiol to initiate preovulatory gonadotrophin surges (McNatty et al., 1985) and (iv) larger secondary preovulatory surges of FSH caused by lower production of inhibin by the ovary (Cahill et al., 1981; Cummins et al., 1983; McNatty et al., 1987). Previous studies have not found a difference in ovarian steroid concentrations or in FSH secretion between Finn ewes and less prolific ewes (e.g. Suffolk: Webb and England, 1984; Wheaton et al., 1988; Galway: Adams et al., 1988). Whether any of the breed or genotype differences in ovulation rate can be explained by differences in FSH isofoms remains to be determined.

Previous studies have emphasized the potential intra-ovarian or paracrine role of the IGFs in regulating follicular growth and differentiation (Hammond et al., 1991) without concern for blood-derived IGFs. Such a paracrine role has been supported by the observations that granulosa cells secrete immunoreactive IGF-1 or IGF-2 or both in vitro (Hsu et al., 1987; Ramasharma and Li, 1987) and that ovarian tissues contain mRNA for IGFs (Voutilainen and Miller, 1987; Murphy et al., 1987; Hernandez et al., 1989; Oliver et al., 1989). However, because the amount of mRNA for IGF-1 is nearly 100-fold greater in the liver than in the ovary (Murphy et al., 1987) and because concentrations of IGF-1 are significantly lower in ovarian follicular fluid than in serum of pigs (Bryan et al., 1989; Spicer et al., 1992a), cattle (Echternamp et al., 1990; Spicer et al., 1991a) and horses (Spicer et al., 1991b), IGF-1 derived from blood serum or plasma must be considered a likely source of intraovarian IGFs. In addition, we and others have observed that IGF-1 concentrations in peripheral and utero-ovarian venous blood during the luteal phase (present study. Expt 2; Jesionowska et al., 1990) and follicular phase (Jesionowska et al., 1990) are similar, and that serum and follicular fluid IGF-1 concentrations are positively correlated (Echternamp et al., 1990; Rabinovici et al., 1991; Spicer et al., 1991b). Thus, further research will be required to determine whether hepatic IGF-1 or ovarian IGF-1 (despite high plasma concentrations) is responsible for stimulating folliculogenesis. Further research will also be required to determine whether the ovary contributes to the increase in plasma IGF-1 observed during the follicular phase of the oestrous cycle in ewes.

In addition to IGFs, the IGF-1-binding proteins have been implicated as potential intra-ovarian regulators of follicular growth and(or) differentiation (Hammond et al., 1991). We observed that plasma IGF-1-binding protein activity did not differ among the various genotypes of ewes, suggesting that plasma IGF-1-binding protein activity is not involved in regulating genotypic differences in ovulation rate. Whether any of the breed or genotype differences in ovulation rate can be explained by differences in intra-ovarian (e.g. follicular fluid) IGF-1-binding protein activity or by differences in the various molecular weight species of the IGF-1-binding proteins remains to be determined.

Studies have demonstrated that there may be genetic determinants of blood concentrations of IGF-1 in mice (Blair et al., 1988; Medrano et al., 1991), pigs (Buonomo et al., 1987), cattle (Echternamp et al., 1990) and humans (Merimee et al., 1982; Suwa et al., 1988). The differences among genetic groups in the present study demonstrate that plasma IGF-1 concentrations are also under genetic control in sheep. The high values for the reproducibility of IGF-1 concentrations in Expt 1 of the present study indicate that differences among individuals are consistent across successive days within an oestrous cycle. We have also observed high (0.68 to 0.74) reproductibilities for IGF-1 concentrations based on one luteal-phase blood sample taken in consecutive cycles of older (20 months) Finn and Cambridge ewes (L. J. Spicer and J. P. Hanrahan, unpublished data). These observations indicate that the relatively large differences among individuals are very consistent over time. The high reproducibility of IGF-1 also suggests that a large portion of the variation in IGF-1 concentrations may be genetic and associated with high heritability. Concentrations of IGF-1 in blood may therefore prove to be a useful tool in genetic selection if genetic correlations with important productivity traits (e.g. growth rate) can be demonstrated. Obviously, from the present study, prolificacy in sheep can be eliminated in this context. Previous studies in mice (Blair et al., 1988) and sheep (Spicer and Zavy, 1992) have demonstrated a link between body weight and IGF-1 concentrations. Similarly, we observed a significant correlation between plasma IGF-1 concentrations and body weights in Finn ewe lambs of Expt 1. However, to establish a definitive role for IGF-1 in growth in ruminants will require further study.

In summary, results from the present study suggest that (i) plasma concentrations of IGF-1 increase during oestrus in cyclic ewes, (ii) plasma concentrations of IGF-1 are influenced by
genotype in sheep but are not genetically associated with ovulation rate. (iii) Plasma IGF-1-binding protein activity is not influenced by stage of cycle or genotype in sheep, and (iv) the ovary does not appear to be a major source of blood IGF-1 during the luteal phase of the oestrous cycle.

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References


Driaucourt MA, Castonguay F, Bindon BM, Piper LR, Quirk JF and Hanrahan JP (1990) Ovarian follicular dynamics in lines of sheep (Finn, Merinos) selected on ovulation rate Journal of Animal Science 60 2034–2041


Hammond JM, Mondschein JS, Samaras SE and Canning SF (1991) The ovarian insulin-like growth factors, a local amplification mechanism for steroidogenesis and hormone action Journal Steroid Biochemistry and Molecular Biology 40 411–418


Hernandez ER, Roberts CT, Jr, LeRoith D and Adashi EY (1989) Rat ovarian insulin-like growth factor-I (IGF-I) gene expression is granulosa cell-selective: 5′-untranslated mRNA variant representation and hormonal regulation Endocrinology 125 572–574


McNatty KP, Hudson N, Henderson KM, Gibb M, Morrison L, Ball K and Smith P (1987) Differences in gonadotrophin concentrations and pituitary responsiveness to GnRH between Booroola ewes which were homozygous (FF), heterozygous (Ff) and non-carriers (+ +) of a major gene influencing their ovulation rate Journal of Reproduction and Fertility 80 577–588


Moses AC, Nissley SP, Passamani J and White RM (1979) Further characterization of growth hormone-dependent somatomedin-binding proteins produced by rat liver cells in culture Endocrinology 104 536–546

Murphy LJ, Bell CL and Friesen HG (1987) Tissue distribution of insulin-like growth factor 1 and II messenger ribonucleic acid in the rat Endocrinology 120 1279–1282


Spicer LJ, Enright WJ, Murphy MG and Roche JF (1991a) Effect of dietary intake on concentrations of insulin-like growth factor-I in plasma and follicular fluid and ovarian function in heifers Domestic Animal Endocrinology 8 433–439


Spicer LJ, Zavy MT, Hanrahan JP and Enright WJ (1991c) Serum concentrations of insulin-like growth factor-I (IGF-I) during the oestrous estrus cycle: effects of genotype and estrus Biology of Reproduction 44 (Supplement 1) 84

Spicer LJ, Klind J, Buonomo FC, Maurer R, Yen JT and Echternkamp SE (1992a) Effect of porcine somatotropin on number of granulosa cells luteinizing...
hormone/human chorionic gonadotropin receptors, oocyte viability, and concentrations of steroids and insulin-like growth factors I and II in follicular fluid of lean and obese gilts Journal of Animal Science 70 3149–3157


Webb R and England BG (1984) Identification of the ovulatory follicle in the ewe: associated changes in follicular size, thecal and granulosa cell luteinizing hormone receptors, antral fluid steroids, and circulating hormones during the preovulatory period Endocrinology 110 873–881
