Premature seasonal inhibition of tonic LH secretion by oestradiol in the female lamb and its consequences

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Summary. Patterns of circulating LH were examined in ovariectomized lambs and adults bearing Silastic capsules containing oestradiol-17β and in untreated ovariectomized lambs. A decrease in serum LH in oestradiol-treated lambs occurred coincidentally with the cessation of ovulations in intact lambs and in the absence of any decrease in circulating LH in untreated ovariectomized lambs. On average, these phenomena occurred 3 weeks before the seasonal reduction in serum LH levels and onset of anoestrus in oestradiol-treated ovariectomized and intact adults, respectively. The results suggest that (1) an early seasonal increase in responsiveness to oestradiol negative feedback on tonic LH secretion is responsible for the premature cessation of ovulations in the lamb, accounting, in part, for the short breeding season during the first year of life and, in some lambs, the failure to initiate cyclicity until the second year after birth; and (2) onset of anoestrum in lambs, in contrast to puberty, is not associated with steroid-independent changes in LH secretion.

Introduction

The breeding season in lambs of several breeds during their first year after birth is much shorter in duration than that of fully mature ewes (Hammond, 1944; Hafez, 1952; Watson & Gamble, 1961; Dyrmundsson, 1973). Not only do lambs attain puberty well after the seasonal onset of ovarian cyclicity in adults, but ovulations in lambs generally cease before those in the adult. Legan, Karsch & Foster (1977) have demonstrated that in the mature female, the increased responsiveness to the suppressive effects of oestradiol on tonic LH secretion is associated with the cessation of the breeding season, i.e. the increase in response to feedback inhibition by oestradiol ultimately prevents occurrence of the normal sequence of preovulatory events. The present study investigated whether the early onset of anoestrum in the lamb is also associated with an early inhibition of LH by oestradiol. A preliminary report has been given (Foster & Ryan, 1979b).

Materials and Methods

Twenty-one Suffolk lambs, born in March 1977, and 21 sexually mature Suffolk ewes (>3 years of age) were studied in natural environmental conditions in Ann Arbor, Michigan (42°18’N latitude). The lambs were the same as those used to study the onset of puberty (Foster & Ryan, 1979a). The diet consisted of hay and was supplemented with a commercial preparation of vitamins and minerals.

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Treatments of lambs and ewes were initiated on 27 July 1977. The ovaries were removed from 10 lambs at midventral laparotomy under pentobarbitone sodium anaesthesia (400 mg i.v.) at 19 weeks of age. Four ovariectomized lambs received no further treatment. In the other 6 lambs, two Silastic capsules (i.d. = 3·4 mm, o.d. = 4·6 mm, Dow-Corning, Midland, Michigan, U.S.A.; Karsch et al., 1973) containing packed column lengths of crystalline oestradiol-17β of 10

![Text-fig. 1](https://example.com/text-fig1.png)

**Text-fig. 1.** Onset of anoestrus (1978) in (a) 10 of 11 March-born lambs and in 16 adult ewes and (b) seasonal change in mean (± s.e.m.) levels of serum LH in 4 ovariectomized (OVX) lambs, in 5 of 6 lambs and 5 adult ewes ovariectomized and treated with oestradiol (E₂). A female was considered to be 'cyclic' until the last ovulation, usually the last oestrus; failure of circulating progesterone concentration to increase to luteal-phase levels at the time of the next two expected ovulations was used as confirmation that the female was anoestrous. One intact lamb failed to ovulate by the end of the study and was excluded from the analysis for average onset of anoestrus (Text-fig. 2, No. 732). One oestradiol-treated ovariectomized lamb failed to exhibit a sustained increase in serum LH (Text-fig. 2, No. 716) and its data are excluded from the average. Undetectable values for serum LH (< 0·25 ng/ml) are depicted by open symbols.
and 15 mm were inserted s.c. at the time of ovariectomy. Five adult females, which had been ovariectomized 3–34 weeks previously, were treated with one 30 mm oestradiol capsule. These treatments produce similar concentrations of circulating oestradiol (3–5 pg/ml) in the lamb (Foster & Ryan, 1979a) and adult (Legan et al., 1977), concentrations which approximate those found during the luteal phase of the oestrous cycle (Hauger, Karsch & Foster, 1977). The capsules remained in situ for the duration of the experiment. One oestradiol-treated ovariectomized lamb failed to exhibit a sustained rise in circulating LH by the end of the study and was excluded from analysis of the seasonal increase in response to oestradiol inhibition.

Eleven untreated intact lambs and 16 adult intact females were used to determine the onset of anoestru in the lamb at the end of the annual breeding season. They were maintained continuously with mature vasectomized rams with painted briskets and were inspected at least once daily for behavioural oestru as evidenced by mating or by paint marks on their hindquarters. Cessation of ovulation was determined by failure of the female to exhibit oestru and by the absence of increased concentrations of serum progesterone typical of a luteal phase (1–3 ng/ml). One lamb failed to ovulate by the end of the study and was excluded from the analysis for onset of anoestru.

Samples of blood (8 ml) were collected by jugular venepuncture between 08:00 and 10:00 h thrice weekly from all 3 groups of lambs, twice weekly from intact adults and weekly from oestradiol-treated ovariectomized adults. Concentrations of LH in serum, expressed in terms of NIH-LH-S12, were determined by a radioimmunoassay (Niswender, Reichtert, Midgley & Nalbandov, 1969) which was modified as described previously (Hauger et al., 1977). Each sample was assayed in duplicate at a volume of 200 μl. When high concentrations of LH were present, the sample was re-assayed in duplicate volumes of 25 μl. Sensitivity, determined as two standard derivations from the buffer control, averaged 0·05 ng which is equivalent to 0·25 ng/ml when 200 μl serum were assayed. Intra-assay variation, determined from the median variance ratio of assay replicates (Duddleson, Midgley & Niswender, 1972), averaged 5% and interassay variation, determined as the coefficient of variation from standard sera quantified in each assay, averaged 12%. Concentrations of progesterone were determined in duplicate in petroleum ether extracts equivalent to 85 μl serum using a previously described radioimmunoassay (Niswender, 1973; Foster, Lemons, Jaffe & Niswender, 1975). Mean extraction recovery was 86%, sensitivity was 0·06 ng/ml, intra-assay variation was 8%, and interassay variation was 11%.

Results

All lambs exhibited their final ovulation before 50% of the adults had become anoestrous (Text-fig. 1a). The mean (± s.e.m.) date of last ovulation in lambs (31 January ± 3 days) occurred 3 weeks earlier than that in adult females (23 February ± 5 days) (P < 0·001, t-test). Similarly, in ovariectomized lambs bearing oestradiol implants, the decrease in LH to low levels (< 1 ng/ml) occurred well before the decrease in serum LH in oestradiol-treated ovariectomized adults (Text-fig. 1b). There was, however, no decrease in mean LH concentrations in untreated ovariectomized lambs (Text-fig. 1b).

Discussion

These results demonstrate that the system governing tonic LH secretion increases its responsiveness to the inhibitory effects of oestradiol earlier in the winter in ewe lambs than in adult ewes. This leads to an earlier reduction in circulating LH concentrations, an earlier failure of preovulatory follicles to develop and hence, premature onset of seasonal anoestru. The sustained high levels of circulating LH in ovariectomized lambs not treated with oestradiol
indicate that during the transition into first anoestrus the ability to secrete LH in the absence of feedback regulation is not impaired. This stands in contrast to the pubertal period when an additional thrust to LH secretion occurs in untreated ovariectomized lambs. Circulating LH rises from low values to those typical of ovariectomized adults concomitant with the pubertal decrease in feedback responsiveness when serum LH increases in oestradiol-treated ovariectomized lambs (Foster & Ryan, 1979a). First anoestrus is therefore precipitated by oestradiol-mediated alterations in tonic LH secretion whereas puberty is associated with both oestradiol-dependent and oestradiol-independent changes in tonic LH secretion. While the significance of such observations remains to be appreciated fully, they suggest that the onset of anoestrus is not simply a reversal of the pubertal process.

In the lambs used in this study, the average duration of the breeding season was 15 ± 1 weeks (i.e. the interval between the first ovulation (18 October ± 7 days; Foster & Ryan, 1979a) and last ovulation (31 January ± 3 days)). This was 10 weeks shorter than the adult breeding season (25 ± 1 weeks; 27 August ± 2 days–23 February ± 5 days). The 3-week earlier cessation of breeding in lambs is therefore only a minor factor in the shorter breeding season, the major

Text-fig. 2. Individual variation in the duration of detectable circulating LH (> 0.25 ng/ml, ●) in oestradiol-treated ovariectomized lambs (Nos 718, 721 and 716) and individual variation in length of breeding season in intact lambs (Nos 717, 728 and 732; △ ovulation without oestrus, ▲ ovulation accompanied by oestrus). Paired observations were made from 6 oestradiol-treated ovariectomized lambs and 11 intact lambs. Details for onset of puberty are reported elsewhere (Foster & Ryan, 1979a).
cause of the abbreviated period of fertility being the failure to attain puberty until 7 weeks after
the onset of breeding by adults (Foster & Ryan, 1979a). However, for some lambs early
seasonal hyper-responsiveness to oestradiol negative feedback may have severe consequences,
e.g. those in which the maturational stimuli driving the pubertal process occur very late in the
autumn and winter breeding season.

The contention that early seasonal inhibition of LH secretion may prevent the onset of
ovulatory cycles in some lambs is developed by consideration of the data presented in Text-fig. 2.
The long period of reduced response to negative feedback in Lamb 718 would presumably have
permitted the occurrence of several ovulations had the ovaries been present as in Lamb 717. A
similar argument may be made for the lamb in which the pubertal reduction in oestradiol
negative feedback responsiveness occurs even later and the seasonal increase in negative
feedback responsiveness earlier (Lamb 721 and Lamb 728). In such females, there would be
adequate time for conception to occur during the first year after birth despite the early cessation
of breeding. However, at the other extreme, in slowly maturing lambs (Text-fig. 2) there may be
insufficient time to overcome completely prepubertal oestradiol inhibition of tonic LH secretion
before the mechanism governing seasonal hyper-responsiveness is prematurely activated.
Ovulation would not occur because circulating LH would not be able to increase sufficiently to
initiate the first follicular phase. This hypothesis would accord with the pattern of circulating LH
in the smallest oestradiol-treated ovariectomized lamb (No. 716) which only exhibited transient
rises in LH and the lack of ovulation in the smallest intact lamb (No. 732) during the first year
after birth. If such a hypothesis proves to be valid, it could provide an explanation for previous
observations that a significant percentage (~20%) of winter- and spring-born lambs (natural
birth season) do not begin oestrous cycles during the first year (Hammond, 1944; Hafez, 1951,
1952; Dyrmundsson & Lees, 1972). The growth rate of such lambs is generally slow.

Text-figure 3 schematically summarizes the foregoing observations and considerations in
terms of responsiveness to oestradiol negative feedback. In the lamb, like the adult, ovulations
are prevented when oestradiol inhibition of tonic LH secretion is high and ovarian cyclicity is
permitted to occur when this inhibition becomes reduced to low levels. Unlike the fully mature

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Text-fig. 3. Schematic illustration of the consequences of premature onset of seasonal anoestrus
in lambs which mature late in the year. The scheme is based upon changes in responsiveness to
oestradiol (E₂) inhibition of tonic LH secretion (a) at the onset and end (anoestrus) of the adult
breeding season and (b) at puberty and first anoestrus in lambs. Reduced LH secretion occurs
when the response to oestradiol negative feedback is high, while increased LH secretion is
permitted when feedback responsiveness is low.
female, however, the developing female is confronted with the challenge to overcome prepubertal hyper-responsiveness to oestradiol negative feedback before the onset of early seasonal hyper-responsiveness. While most lambs are successful in this regard and ovulations are initiated during the first year, albeit late in some females, others are not and they remain anovulatory until the following year.

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References


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