PROCEEDINGS OF THE NUTRITION SOCIETY
A Scientific Meeting was held at the University of Nottingham on 12–15 July 1993

Symposium on
'Reproduction and fertility'

The role of nutrition and photoperiod in the timing of puberty

BY CLARE L. ADAM AND JOHN J. ROBINSON
Rowett Research Institute, Bucksburn, Aberdeen AB2 9SB

In animals that are kept in temperate latitudes and that are seasonal in their breeding activity, nutritional and photoperiodic signals operate in harmony to time the activation of the gonadotrophin-releasing hormone (GnRH) pulse generator in the brain and trigger puberty. These signals ensure that within the constraints imposed by the circannual changes in the environment, body size and time of puberty are appropriate for the overall success of the reproductive process.

Although photoperiodic influences on the timing of puberty in farmed species occur in sheep (Foster *et al.* 1986), goats (Deveson *et al.* 1992), red deer (*Cervus elaphus*; Webster & Barrell, 1985), cattle (Schillo *et al.* 1992) and pigs (Paterson *et al.* 1992), it is the short-day breeders (sheep, goats and red deer) that are most photodependent. If the natural timings of their birth during either the increasing daylength of the spring (sheep, goats) or the long days of early summer (red deer) are followed by natural photoperiodic changes and normal growth rates then puberty usually occurs during the declining daylengths of either the first (sheep, goats) or second (red deer) autumn. Recent studies for all three species, and in particular for sheep and deer, have added to our understanding of the interdependence of nutrition and photoperiod in the timing of puberty. These have varied from empirical descriptions of the effects of restricted growth rates and artificial photoperiods on the activation of the GnRH pulse generator in both the female and male, to mechanistic approaches which attempt to identify the bio-chemical and molecular signals involved in recording and transmitting metabolic information on nutritional status and photoperiod history to the neuroendocrine axis.

Recent research also involves attempts to identify blood-borne metabolites that mediate the nutritional activation of the GnRH pulse generator. In the case of photoperiod, for which there is unequivocal proof that the mediator of this environ-mental cue in timing puberty is the pineal indoleamine, melatonin (Yellon & Foster, 1986), research effort is now directed to identifying its receptor sites and mode of action. In this regard the recent observations that sheep and deer possess melatonin receptors during fetal life (Helliwell & Williams, 1991; Helliwell *et al.* 1991) are particularly interesting in view of the demonstration that the photoperiodic signal received by the fetus *in utero* can alter age at puberty in both species (Adam *et al.* 1992*a*; Helliwell *et al.* 1992), albeit in ways that are specific for each sex.

NUTRITION, PHOTOPERIOD INTERACTIONS OR THE COORDINATION OF SIZE AND SEASON

Spring-born ewe lambs provide an excellent illustration of the interdependence of size and season on the attainment of puberty. Those grown rapidly achieve puberty in their first autumn and at a younger age and heavier weight than those subjected to transitory periods of food restriction. A protracted period of food restriction from mid-summer to mid-winter, followed by *ad lib.* feeding to achieve the threshold size for puberty in the subsequent spring, delays puberty until the shortening daylengths of the following autumn (Foster *et al.* 1985). Autumn-born ewe lambs that are grown rapidly invariably fail to achieve puberty in their first winter and have to wait until the following autumn for the acquisition of the photoperiodic information that is needed for the activation of the GnRH pulse generator (Foster, 1981). This dependence on a photoperiodic cue, inevitably leads to pubertal sizes that vary enormously (32–50 kg in the breed used by Foster *et al.* 1985). Nonetheless, for a specific photoperiodic regimen there is no evidence that the fatness or protein content of the body are important mediators of sexual maturity in the female lamb (Moore *et al.* 1985), nor indeed is body weight *per se* (Suttie *et al.* 1991*a*). In the early observations of Keane (1974) the threshold body weight for puberty in spring-born ewe lambs grown at different rates declined from 40 kg in early November to 33 kg in late December, again casting doubt on the concept of a uniform threshold body weight for the attainment of puberty, but not excluding the idea of a critical minimum weight for puberty, as exemplified by Hamilton & Blaxter (1980) in farmed red deer hinds kept in a hill environment. However, in the red deer, if this critical weight is exceeded by means of experimentally-advanced (February) birth dates, puberty is expressed in the first rather than the usual second autumn of life (Adam *et al.* 1992*b*).

For spring-born ewe lambs, the key features of the natural photoperiod that interact with unrestricted growth to time puberty at about 30 weeks of age are the initial long days of summer followed by the declining daylength of autumn (Foster *et al.* 1986). Continuous exposure to long days prevents puberty in the first autumn but does not block it indefinitely (Ebling & Foster, 1988) and the same is true in spring-born lambs exposed continuously to short days. For lambs on short days, exposure to a 10-week period of long days starting at 12 weeks of age or a 5-week period at 17 weeks of age, followed in both cases by a return to short days, initiates oestrus cyclicity at the normal age (Foster *et al.* 1986). Indeed transitory exposure to long days for as little as 1 week at 21 weeks of age also initiates oestrus at the usual age, albeit somewhat abnormally in that there is a high incidence of short luteal phases (Yellon & Foster, 1985). In contrast, when the transitory period of exposure to long days is imposed at an earlier age (5–10 weeks), it is ineffective, leading Foster *et al.* (1986) to suggest that at very young ages the circadian melatonin rhythm may not be fully entrained to the light–dark cycle. Sequential observations made by Rodway *et al.* (1985) showing that the night-time rise in melatonin is most pronounced around the time of puberty provide some support for this suggestion. However, more recent observations of Foster *et al.* (1989*a*) indicate that it is not the low-amplitude melatonin rhythm of the neonatal lamb that limits the induction of puberty by seasonal light cues but rather immaturity of the reproductive axis or inadequate somatic development.

An age-dependent response also occurs when spring-born female lambs are exposed to artificial short days or are implanted with melatonin to mimic a short-day effect. For example, the insertion of melatonin implants at 19 weeks of age advanced the time of

puberty by 5·2 weeks but was without effect when carried out at 7·5 weeks (Nowak & Rodway, 1985); for ewe lambs implanted at birth, puberty was delayed by 4 weeks (Kennaway *et al.* 1986). Similarly in red deer, which reach puberty naturally in their second autumn, Webster & Barrell (1985), Adam *et al.* (1989), Asher (1990) and Fisher *et al.* (1990) have demonstrated that there is exquisite sensitivity in the timing of melatonin treatment for the induction of precocious puberty.

In the male lamb, nutritional influences play a similar role to that in the female, with those on high planes of nutrition achieving puberty at younger ages and heavier body weights than those on low planes of nutrition. However, compared with the female, photoperiod plays a relatively minor role in the attainment of puberty in the male (Dýrmundsson, 1987). For example, spermatogenesis begins in spring-born ram lambs during mid-summer, approximately 20 weeks ahead of puberty in the female and before the natural decline in daylength. Using the initiation of a sustained increase in luteinizing hormone (LH) secretion as a more sensitive indicator of puberty, Wood *et al.* (1991*b*) have demonstrated that neuroendocrine sexual maturity occurs in the male at 5–6 weeks of age under natural photoperiod and is only delayed by approximately 3 weeks under reverse photoperiod.

GESTATIONAL PHOTOPERIOD AND THE TIMING OF PUBERTY

The lamb develops a circadian rhythm of melatonin in the first few weeks of life that accurately reflects the ambient photoperiod (Claypool *et al.* 1989) and appears, on the basis of a shift in prolactin concentrations, to be able to discern changes in daylength imposed as early as 7 d following birth (Ebling *et al.* 1988). However, there is also evidence of an earlier ability to perceive photoperiodic information. In the pregnant ewe, melatonin of maternal origin crosses the placenta and gives rise to a diurnal pattern of circulating melatonin concentrations in the fetus (Yellon & Longo, 1987, 1988; Zemdegs *et al.* 1988). In so far as melatonin influences prolactin secretion, fetal prolactin concentrations indicate that the fetus can respond to the maternal melatonin signal (Bassett *et al.* 1989; Serrón-Ferré *et al.* 1989). Furthermore, specific melatonin-binding sites have been identified in the brains of fetal sheep (Helliwell & Williams, 1991) and red deer (Helliwell *et al.* 1991) as early as days 40 and 66 of gestation respectively.

Evidence that the neonate utilizes the maternal photoperiod in its acquisition of a 'photoperiodic history' comes from the profound influence of prenatal photoperiod on prolactin secretion in the newborn sheep (Ebling *et al.* 1989*b*) and red deer (Adam *et al.* 1992*c*). Thus, while circulating prolactin concentrations in both species at birth reflect the maternal photoperiodic signal, the subsequent response of the newborn to an alteration in photoperiod is governed by the photoperiodic information received *in utero*. Although there appears to be no effect of gestational photoperiod on the subsequent growth rates of the lamb (Bassett, 1992) or red deer calf (Adam *et al.* 1992*c*), evidence is accumulating in both species for an influence on the rate of sexual maturation. Such an influence has been demonstrated in some rodent species with short intervals to puberty, e.g. the meadow vole (*Microtus pennsylvanicus*; Lee *et al.* 1987) and the Djungarian hamster (*Phodopus sungorus sungorus*; Stetson *et al.* 1986), but up to now results from large animal species have been equivocal. For example, in the ewe lamb, Sunderland *et al.* (1990) and Herbosa & Foster (1992) found no effect of prenatal photoperiod on the timing of puberty, whereas Helliwell *et al.* (1992) reported that prenatal long days could

facilitate the induction of puberty by an early postnatal decrease in daylength. Adam *et al.* (1992*a*) have demonstrated advanced puberty in male red deer whose mothers were kept in long days as opposed to short days during pregnancy but the same treatment did not affect puberty in contemporary female offspring (C. L. Adam, C. E. Kyle & P. Young, unpublished results). For autumn-born goats Deveson *et al.* (1992) reported that exposure to long days for a 2-month period before birth, followed by a return to the ambient photoperiod after birth, delayed the timing of puberty in both males and females. The apparent conflict may be due to the variety of photoperiodic regimens used, ruling out direct comparisons between results. For example, the spring-born female lamb receiving adequate stimulatory photoperiodic cues from its natural postnatal exposure to long days followed by short days may not be reliant on its prenatal photoperiodic history. On the other hand, the photoperiodic experience *in utero* may be more critical in the male since sexual maturation is initiated much earlier and appears to involve prenatal programming by androgens (Wood *et al.* 1991*a*).

ACTIVATION OF THE GnRH PULSE GENERATOR

Unravelling the way in which nutrition and photoperiod initiate the rapid LH pulses that trigger puberty is proving a major research challenge. Although the enhanced LH pulsing merely reflects the increased activity of the hypothalamic GnRH pulse generator, the immediate prepubertal timing of this activity does not occur until long after the hypothalamic–pituitary system is capable of sustaining high-frequency LH pulses. For example, female lambs have the ability to produce high-frequency pulses within a few weeks following birth (Foster *et al.* 1986) yet fail to do so until nutritional and photoperiodic cues are appropriate. Similarly the ovaries of the young lamb are capable of ovulating in response to exogenously-administered gonadotrophin before the normal time of puberty (Dýrmundsson, 1987); so too are the ovaries of older lambs rendered reproductively inactive by either chronic undernutrition or an inhibitory photoperiod (McShane & Keisler, 1991).

Progress towards a mechanistic understanding of the pubertal activation of the GnRH pulse generator comes from studies on ovariectomized female lambs with or without oestradiol implants. This experimental model demonstrates that ovarian oestradiol, via alterations in its inhibitory feedback action on the hypothalamus, plays an important role in mediating the pubertal stimulation of the GnRH pulse generator by nutrition and photoperiod (Foster *et al.* 1986). During periods of exposure to inadequate nutrition or an inhibitory photoperiod, failure to achieve puberty arises from the maintenance of a heightened sensitivity of the GnRH pulse generator to the negative feedback effect of oestradiol. In the presence of a permissive photoperiodic cue, improved nutrition is accompanied by a rapid decrease in the negative feedback action of oestradiol and the initiation of rapid LH pulses which trigger puberty (Foster *et al.* 1986). This ability of the hypothalamic–pituitary axis to respond quickly to an improved nutritional status implies that during periods of undernutrition the ewe lamb is capable of monitoring the important pubertal-dependent components of its photoperiodic environment.

In the chronically undernourished ovariectomized female lamb in which puberty is delayed, exogenously administered GnRH at physiological doses (2·5 mg/kg body weight) induces LH secretion, thus proving pituitary competence (Foster *et al.* 1989*b*).

Similarly the hypothalamus has an adequate supply of GnRH which can be released by an intravenous injection of N-methyl-D-aspartate (NMDA) which is an agonist of the stimulatory neurotransmitter, glutamate (Ebling *et al.* 1990*b*). Provided the nutritionally-restricted ovariectomized lamb has been subjected to the stimulatory photoperiodic cue of long followed by short days during the period of food restriction, its realimentation is accompanied within 1–2 weeks, and in some individuals within 2 d, by increases in the pituitary synthesis of LH as measured by the amounts of mRNA, and increases in LH secretion as detected by circulating plasma concentrations (Landefeld *et al.* 1989). Interestingly, parenteral infusion of a dextrose–amino acid mixture is as effective as high-plane feeding in sustaining an established pattern of enhanced LH secretion (Foster *et al.* 1988).

The gonadectomized model has been used also to demonstrate sexual differentiation in the timing of the responsiveness of the hypothalamic–pituitary axis to oestradiol inhibition. Male lambs castrated at 2 weeks of age and implanted with oestradiol exhibit rapid LH pulses at a time (8–11 weeks of age) that coincides with increased testicular growth rates and the onset of spermatogenesis in intact controls (Claypool & Foster, 1990), and some 18 weeks ahead of the decreased responsiveness to oestradiol that coincides with the onset of ovulatory cycles in the female exposed to a stimulatory photoperiod. However, gonadectomy without oestradiol is accompanied by a higher frequency of LH pulses during sexual development in males than females, implying that sexual differentiation may also occur at a steroid-independent level (Claypool & Foster, 1990). While these results suggest a direct drive by the central nervous system on gonadotrophin secretion this may be an oversimplification. A steroid-independent effect on LH secretion occurs in gonadectomized female lambs reared under an inhibitory photoperiod, but in this case their age-related increase in LH pulse frequency in the absence of oestradiol is not accompanied by a decreased responsiveness of their hypothalamic–pituitary axis to oestradiol inhibition (Ebling *et al.* 1990*a*).

Recent attempts to unravel the mechanisms controlling the early activation of the GnRH pulse generator in the male have also used the 'gonadectomized–oestradiol implant' model and have provided an intriguing insight into the role of prenatal programming in timing puberty. Female lambs born to pregnant ewes that were injected weekly with 100 mg testosterone cypionate from 30 to 90 d of gestation were gonadectomized at 2 weeks of age and implanted with oestradiol. These lambs exhibited precocious development of their hypothalamic–pituitary axis as exemplified by an early increase in LH secretion which coincided with that observed in untreated contemporary males (Wood *et al.* 1991*a*).

In all the preceding studies, either the elevation of LH or the increase in its frequency of episodic release are indicative of an increase in the activity of the GnRH pulse generator and the attainment of puberty. However, the associated changes in follicle-stimulating hormone (FSH) have also been investigated. For example, in the study of Landefeld *et al.* (1989) involving non-oestradiol-treated ovariectomized lambs, the amounts of FSHβ mRNA as well as LHα and LHβ mRNA were increased following realimentation and so too were the circulating concentrations of immunoreactive FSH. Using this same experimental animal model, Padmanabhan *et al.* (1989) found that, following a period of nutritionally-imposed growth retardation, realimentation was accompanied by increases of 2- and 3-fold in immunoreactive and bioactive FSH respectively. Furthermore, in contrast to the realimentation-induced increases in LH

pulse frequency, FSH pulse frequency remained constant but pulse amplitude increased, with the bioactive pulse amplitudes being almost 60% higher than those of the immunoreactive. More recently, Padmanabhan *et al.* (1992) confirmed in ovary-intact lambs that puberty was characterized by higher circulating concentrations of bioactive FSH and these were associated with an increase in the proportion of less acidic FSH isoforms in plasma, thereby implying that alterations in FSH heterogeneity may be involved in initiating puberty. In contrast, the exogenous administration of GnRH to growth-restricted ovariectomized lambs did not alter either pituitary or serum FSH heterogeneity (Hassing *et al.* 1993).

Whether the natural activation of the GnRH pulse generator at puberty leads to heterogeneity of the gonadotrophins that is critical to the attainment of reproductive competence is still a matter of conjecture. It is clear, however, that in order to attain puberty neither nutritional nor photoperiodic cues take priority but both are required to be stimulatory. The chronically-undernourished female lamb has an unimpaired melatonin mechanism to monitor daylength but can only respond to stimulatory photoperiods when her body size is adequate (Foster & Yellon, 1985). Conversely, the stimulatory effects of increased nutrient intake on LH secretion can be prevented by the inhibitory effects of an inappropriate photoperiodic history (McShane & Keisler, 1991). In many instances the activation of the GnRH system by nutrition is very rapid, implicating the existence of some specific blood-borne metabolite that relays information on the shift in nutritional status directly to the hypothalamus. For photoperiodic information a protracted programming period is required and for this there is unequivocal evidence that the mediator is the pineal indoleamine, melatonin.

PHOTOPERIODIC INFORMATION AND THE MELATONIN SIGNAL

Melatonin (5-methoxy-N-acetyltryptamine) is synthesized and secreted in a precise circadian rhythm. Concentrations in peripheral plasma are elevated during darkness and the duration of their normal elevation is directly proportional to the length of the dark phase, thereby providing the animal with a precise record of its photoperiodic environment (Reiter, 1991). In seasonal breeders the accumulated melatonin signal controls the timing of puberty in both long- and short-day breeders. It is, therefore, neither pro- nor anti-gonadotrophic. Although its mode of action in timing the activation of the GnRH pulse generator is not yet known, melatonin receptors have been identified in the *pars tuberalis* (PT) of the ovine pituitary during both adult (Morgan & Williams, 1989) and fetal life (Helliwell & Williams, 1991). Within the PT the melatonin-responsive cells are secretory in type (Morgan *et al.* 1991) and in view of the ability of melatonin to influence the nature of their secretions (Morgan *et al.* 1992) it has been postulated that these may be involved either directly or indirectly in the timing of the activation of the GnRH pulse generator by a permissive photoperiod (Morgan *et al.* 1992). Following the demonstration by Helliwell *et al.* (1992) that the prenatal photoperiod of the ovine fetus influences the timing of puberty, it has been suggested by Skinner *et al.* (1993) from their finding that melatonin inhibits LH-releasing hormone (LHRH)-stimulated LH release *in vitro* from the fetal ovine PT, that this may represent a mechanism whereby the melatonin signal influences the timing of puberty in the ewe lamb.

NUTRITIONAL STATUS AND ITS METABOLIC SIGNALS

Because of the well-recognized inhibition of the GnRH pulse generator by under-nutrition and its rapid activation following realimentation, this model is often used in attempts to identify blood-borne metabolites of nutritional origin that act either directly or indirectly on the neuroendocrine system. Concern that the model may reflect non-specific inputs associated with the psychological stress of food restriction, rather than specific metabolic factors related to current nutrition, has been allayed by the recent studies of Schreihofer *et al.* (1993*a*,*b*). Nonetheless, in interpreting the available information it must be appreciated that acute signalling of nutrient status may differ dramatically from the longer-term signalling that is related to growth (Bronson & Manning, 1988) and that normal control mechanisms may become intertwined with pathophysiological mechanisms arising from long-term undernutrition.

Metabolic cues are likely to be metabolic hormones or products of the pathways that they regulate. The alleviation of undernutrition-suppressed LH secretion by increasing feed intake occurs independently of body weight (Foster *et al.* 1989*b*; Suttie *et al.* 1991*a*) and can be mimicked by parenteral infusion of glucose and/or a mixture of amino acids (I'Anson *et al.* 1991) or abomasal infusion of a single amino acid, tyrosine (Hall *et al.* 1992). Insulin, stimulated by glucose administration and suppressed by undernutrition, may be a candidate for metabolic signalling in that it can also influence the availability of neurotransmitter substrates involved in GnRH secretion (Steiner, 1987) and has, in some experiments, led to enhanced ovulation rates in sheep and pigs (for review, see Robinson, 1990). However, its exact role is unclear since LH secretion in the growth-restricted female lamb was not altered by parenteral (Suttie *et al.* 1991*a*) or intra-cerebroventricular (Hileman *et al.* 1990) infusion of insulin, although the latter route decreased LH pulsatility in lambs fed *ad lib*.

The obvious association between growth and puberty has led to the postulate that growth hormone (GH) is involved; however, all the available evidence suggests that such a role is not primary. In humans, GH is normally elevated during puberty but its precise action on the reproductive axis remains unclear (Ogilvy & Shalet, 1992). Whereas, in rats, secretion of both LH and GH is diminished by chronic low nutrition (Sisk & Bronson, 1986), LH secretion is reduced but GH secretion increased in the nutritionally growth-retarded lamb (Foster *et al.* 1989*b*); and LH secretion increases and GH secretion decreases in the lamb on realimentation. Moreover, there is apparently no pubertal GH rise in female sheep (Suttie *et al.* 1991*b*) and administration of exogenous GH fails to alter the timing of puberty (Bucholtz *et al.* 1990; Suttie *et al.* 1991*b*).

The role of the GH-controlled insulin-like growth factor-1 (IGF-1) deserves some attention since circulating levels are elevated during puberty in rodents and primates (Copeland *et al.* 1982; Handelsman *et al.* 1987). Furthermore, Hiney *et al.* (1991) demonstrated a direct stimulatory effect of IGF-1 on LHRH release when administered to prepubertal rats in the region of the GnRH nerve terminals in the median eminence of the hypothalamus, implying that it may be a metabolic signal involved in regulating sexual maturation. However, there is no evidence for a pubertal rise in IGF-1 in female sheep (Suttie *et al.* 1991*b*) and the pubertal breeding season of male deer occurs when peripheral IGF-1 concentrations have decreased following a period of elevation associated with the spring–summer growth spurt of red deer (Suttie *et al.* 1989) and of reindeer (Suttie *et al.* 1991*c*). In contrast, IGF-1 is elevated during the steroid-dependent pubertal growth spurt in humans. The significance of these species and/or sex differences in the

temporal pattern of IGF-1 is not clear. However, IGF-1 may have a different role or have its effects masked in seasonal v. non-seasonal breeders, and there are clearly sex differences in the timing of the initiation as opposed to the culmination of pubertal development (Claypool & Foster, 1990). Perhaps of particular relevance to seasonal breeders are the intriguing observations that IGF-1 concentrations are also sensitive to photoperiod. For example, in the reindeer, a short-day breeder, Suttie et al. (1991c) found elevated IGF-1 concentrations during long days and in the hamster, a long-day breeder, Vriend et al. (1988) reported that injecting melatonin to mimic a short-day effect also increased IGF-1 concentrations. Thus in both species elevated IGF-1 concentrations occurred during their inhibitory photoperiod, making it difficult to dismiss a role for this hormone in the nutritional mechanisms that influence the timing of puberty.

A relationship between thyroid function and growth is well established and both hypo- and hyperthyroidism delay puberty in the ram lamb by reducing hypothalamic GnRH release (Chandrasekhar et al. 1985, 1986). However, there is no further evidence that thyroid secretions provide a primary metabolic cue for puberty, although they do play an active role in terminating the breeding season in female sheep (Nicholls et al. 1988) and in initiating sexual quiescence in red deer stags (Shi & Barrell, 1992) since T4 is essential for ensuring the shift in steroid negative feedback that is required to inactivate the GnRH pulse generator (Webster et al. 1991).

NEUROTRANSMITTER MECHANISMS AND THE PUBERTAL ACTIVATION OF THE GnRH PULSE GENERATOR

A number of neurotransmitters have been implicated in the activation of the GnRH pulse generator but those involved specifically in mediating nutritional and photo-periodic information are still a matter of conjecture. Some amino acids can act directly as neurotransmitters or indirectly, following metabolism, e.g. glutamine and its metabolite γ-aminobutyric acid (GABA), tyrosine and the catecholamines. Opioid peptides also act as neurotransmitters and their location in the diencephalon is in keeping with their role in the control of gonadotrophin secretion (Thiéry & Martin, 1991). Neurotransmitter mechanisms involve both inhibitory and stimulatory pathways and it may well be the changing balance between these that determines the timing of puberty. For example, the opioids are involved in GnRH inhibition, glutamine and aspartate in GnRH stimulation and the catecholamines in both.

Elevation of LH concentrations following the administration of the opiate antagonist naloxone is the accepted bioassay for the opioidergic inhibition of the GnRH pulse generator. It is well established that endogenous opioids are involved in the steroid feedback inhibition of GnRH secretion in non-seasonal breeders (Malven, 1986). They are also involved in steroid-dependent LH inhibition in the seasonally-breeding sheep, but only during the sexually active phase of the annual cycle when daylengths are short (Lincoln et al. 1987). However, in the prepubertal ewe lamb pulsatile LH secretion is inhibited by endogenous opioids with or without ovarian steroid feedback (Ebling et al. 1989a) implying the existence of both direct and indirect effects on the pulse generator. Various workers have attempted to correlate changes in opioid inhibition with the pubertal transition but there is insufficient evidence to suggest a causal role. Whereas Rawlings & Churchill (1990) reported an absence of opioidergic LH suppression in very

young ewe lambs, Ebling *et al.* (1989*a*) found no change in responses to naloxone during reproductive maturation. Similarly no pubertal decline in opioid inhibition has been reported for heifers (Wolfe *et al.* 1992) and bull calves (Rodriguez *et al.* 1993). The disappearance of opioid inhibition, i.e. absence of effect of naloxone on LH, in the underfed hypogonadotropic prepubertal ewe (Ebling *et al.* 1990*b*; Recabarren *et al.* 1990) and gilt (Cosgrove *et al.* 1991) further rules out a role for opiates as 'metabolic messengers' during dietary restriction.

Stimulation of the neurostimulatory amino acids, glutamine and aspartate by the agonist, N-methyl-D-aspartate (NMDA) induces increased LH secretion in the prepubertal ewe lamb (I'Anson *et al.* 1993). This effect is not blocked during nutritional growth restriction (Ebling *et al.* 1990*b*) or by inhibitory photoperiod (Jansen *et al.* 1991; Lincoln & Wu, 1991). However, NMDA does not consistently stimulate LH release, the response being largely 'all-or-none' rather than dose-dependent, leading I'Anson *et al.* (1993) to postulate that both stimulatory and inhibitory pathways may be activated, with the dominant pathway dictating the level of reproductive activity. Onset of puberty may then be associated with increased direct glutamate–aspartate stimulatory neurotransmitter input to the GnRH pulse generator, and reproductive quiescence with the activation of inhibitory neurotransmitters such as opiates (sheep, Lincoln & Wu, 1991; rhesus monkey, Reyes *et al.* 1991).

The catecholamines are undoubtedly involved in the control of GnRH release (Thiéry & Martin, 1991) but whether their role in timing puberty is inhibitory or stimulatory is not clear. Dopaminergic inhibition of LH release has been demonstrated in the prepubertal lamb (Brango *et al.* 1990), yet increased dopaminergic neuronal activity in the hypothalamus has been linked with increased LH secretion in the pubertal bull calf (Rodriguez *et al.* 1993). Noradrenergic inputs have been reported to be stimulatory to LH release (Terasawa *et al.* 1988) whereas serotonergic pathways are inhibitory (Mondragon *et al.* 1986). Catecholaminergic systems are sensitive to steroids and may be responsible for mediating ovarian steroid inhibition, while steroid-independent effects appear to be mediated by a serotonergic pathway (Meyer & Goodman, 1986). Clearly there are several catecholaminergic pathways that may be involved in the pubertal process; however, their complex interactions, including those with other neurotransmitters such as opioids, have yet to be unravelled. The identification of the metabolic cues and neurotransmitter pathways that transport nutritional and photoperiodic information to the hypothalamic GnRH pulse generator and, thereby, initiate the pubertal process are now major research challenges.

REFERENCES

Adam, C. L., Kyle, C. E. & Young, P. (1992*a*). Prenatal photoperiod influences timing of puberty in red deer. *Journal of Reproduction and Fertility Abstract Series* no. 9, Abstr. 5.

Adam, C. L., Kyle, C. E. & Young, P. (1992*b*). Growth and reproductive development of red deer calves (*Cervus elaphus*) born out-of-season. *Animal Production* **55**, 265–270.

Adam, C. L., Kyle, C. E. & Young, P. (1992*c*). Influence of prenatal photoperiod on postnatal prolactin secretion in red deer (*Cervus elaphus*). *Journal of Reproduction and Fertility* **95**, 959–964.

Adam, C. L., Moir, C. E. & Shiach, P. (1989). Effect of melatonin on puberty in female red deer. *Journal of Reproduction and Fertility Abstract Series* no. 3, Abstr. 110.

Asher, G. W. (1990). Effect of subcutaneous melatonin implants on the seasonal attainment of puberty in female red deer (*Cervus elaphus*). *Animal Reproduction Science* **22**, 145–159.

Bassett, J. M. (1992). Effects of additional lighting to provide a summer photoperiod for winter-housed pregnant ewes on plasma prolactin, udder development and lamb birthweight. *Journal of Agricultural Science, Cambridge* **119**, 127–136.

Bassett, J. M., Curtis, N., Hanson, C. & Weeding, C. M. (1989). Effects of altered photoperiod or maternal melatonin administration on plasma prolactin concentrations in fetal lambs. *Journal of Endocrinology* **122**, 633–643.

Brango, C. W., Whisnant, C. S. & Goodman, R. L. (1990). A role for catecholaminergic neurons in suppression of pulsatile luteinizing hormone secretion in the prepubertal ewe lamb. *Neuroendocrinology* **52**, 448–454.

Bronson, F. H. & Manning, J. M. (1988). Food, energy expenditure and puberty in female rats. *Proceedings of the 11th International Congress on Animal Reproduction and Artificial Insemination, Dublin*, pp. 110–116.

Bucholtz, D. C., Suttie, J. M., Kostyo, J., Adel, T., Ebling, F. J. P. & Foster, D. L. (1990). Is growth hormone an important cue timing puberty in the female lamb? *Biology of Reproduction* **42**, Suppl. 1, Abstr. 18.

Chandrasekhar, Y., D'Occhio, M. J., Holland, M. K. & Setchell, B. P. (1985). Activity of the hypothalamo–pituitary axis and testicular development in prepubertal ram lambs with induced hypothyroidism or hyperthyroidism. *Endocrinology* **117**, 1645–1651.

Chandrasekhar, Y., D'Occhio, M. J. & Setchell, B. P. (1986). Delayed puberty caused by hyperthyroidism in ram lambs is not a result of suppression in body growth. *Journal of Reproduction and Fertility* **76**, 763–769.

Claypool, L. E. & Foster, D. L. (1990). Sexual differentiation of the mechanism controlling pulsatile secretion of luteinizing hormone contributes to sexual differences in the timing of puberty in sheep. *Endocrinology* **126**, 1206–1215.

Claypool, L. E., Wood, R. I., Yellon, S. M. & Foster, D. L. (1989). The ontogeny of melatonin secretion in the lamb. *Endocrinology* **124**, 2135–2143.

Copeland, K. C., Kuehl, T. J. & Castracane, V. D. (1982). Pubertal endocrinology of the baboon: Elevated somatomedin-C/insulin-like growth factor 1 at puberty. *Journal of Clinical Endocrinology and Metabolism* **55**, 1198–1201.

Cosgrove, J. R., Booth, P. J. & Foxcroft, G. R. (1991). Opioidergic control of gonadotrophin secretion in the prepubertal gilt during restricted feeding and realimentation. *Journal of Reproduction and Fertility* **91**, 277–284.

Deveson, S., Forsyth, I. A. & Arendt, J. (1992). Retardation of pubertal development by prenatal long days in goat kids born in autumn. *Journal of Reproduction and Fertility* **95**, 629–637.

Dýrmundsson, Ó. R. (1987). Advancement of puberty in male and female sheep. In *New Techniques in Sheep Production*, pp. 65–76 [I. Fayez, M. Marai and J. B. Owen, editors]. London: Butterworths.

Ebling, F. J. P., Claypool, L. E. & Foster, D. L. (1988). Neuroendocrine responsiveness to light during the neonatal period in the sheep. *Journal of Endocrinology* **119**, 211–218.

Ebling, F. J. P. & Foster, D. L. (1988). Photoperiod requirements for puberty differ from those for the onset of the adult breeding season in female sheep. *Journal of Reproduction and Fertility* **84**, 283–293.

Ebling, F. J. P., Kushler, R. H. & Foster, D. L. (1990*a*). Pulsatile LH secretion during sexual maturation in the female sheep: photoperiodic regulation in the presence and absence of ovarian steroid feedback as determined in the same individual. *Neuroendocrinology* **52**, 229–237.

Ebling, F. J. P., Schwartz, M. L. & Foster, D. L. (1989*a*). Endogenous opioid regulation of pulsatile luteinizing hormone secretion during sexual maturation in the female sheep. *Endocrinology* **125**, 369–383.

Ebling, F. J. P., Wood, R. I., Karsch, F. J., Vannerson, L. A., Suttie, J. M., Bucholtz, D. C., Schall, R. E. & Foster, D. L. (1990*b*). Metabolic interfaces between growth and reproduction. III. Central mechanisms controlling pulsatile luteinizing hormone secretion in the nutritionally growth-limited female lamb. *Endocrinology* **126**, 2719–2727.

Ebling, F. J. P., Wood, R. I., Suttie, J. M., Adel, T. E. & Foster, D. L. (1989*b*). Prenatal photoperiod influences neonatal prolactin secretion in the sheep. *Endocrinology* **125**, 384–391.

Fisher, M. W., Fennessy, P. F. & Johnstone, P. D. (1990). The timing of melatonin treatment affects the seasonal onset of ovarian activity, coat growth and live weight in young red deer hinds. *Animal Reproduction Science* **23**, 49–59.

Foster, D. L. (1981). Mechanism for delay of first ovulation in lambs born in the wrong season (fall). *Biology of Reproduction* **25**, 85–92.

Foster, D. L., Ebling, F. J. P., Claypool, L. E., Wood, R. I., Adel, T. E. & Schramm, W. (1989*a*). Amplitude modulation of the nightly melatonin rise in the neonatal lamb and the subsequent timing of puberty. *Biology of Reproduction* **40**, 920–928.

Foster, D. L., Ebling, F. J. P., Micka, A. F., Vannerson, L. A., Bucholtz, D. C., Wood, R. I., Suttie, J. M. & Fenner, D. E. (1989b). Metabolic interfaces between growth and reproduction. I. Nutritional modulation of gonadotropin, prolactin and growth hormone secretion in the growth-limited female lamb. *Endocrinology* **125,** 342–350.

Foster, D. L., Ebling, F. J. P., Vannerson, L. A., Bucholtz, D. C., Wood, R. I. & Micka, A. F. (1988). Modulation of gonadotropin secretion during development by nutrition and growth. *Proceedings of the 11th International Congress on Animal Reproduction and Artificial Insemination, Dublin,* pp. 101–108.

Foster, D. L., Karsch, F. J., Olster, D. H., Ryan, K. D. & Yellon, S. M. (1986). Determinants of puberty in a seasonal breeder. *Recent Progress in Hormone Research* **42,** 331–378.

Foster, D. L. & Yellon, S. M. (1985). Photoperiodic time measurement is maintained in undernourished lambs with delayed puberty. *Journal of Reproduction and Fertility* **75,** 203–208.

Foster, D. L., Yellon, S. M. & Olster, D. H. (1985). Internal and external determinants of the timing of puberty in the female. *Journal of Reproduction and Fertility* **75,** 327–344.

Hall, J. B., Schillo, K. K., Hileman, S. M. & Boling, J. A. (1992). Does tyrosine act as a nutritional signal mediating the effects of increased feed intake on luteinizing hormone patterns in growth-restricted lambs? *Biology of Reproduction* **46,** 573–579.

Hamilton, W. J. & Blaxter, K. L. (1980). Reproduction in farmed red deer. 1. Hind and stag fertility. *Journal of Agricultural Science, Cambridge* **95,** 261–273.

Handelsman, D. J., Spaliviero, J. A., Scott, C. D. & Baxter, R. C. (1987). Hormonal regulation of the peripubertal surge of insulin-like growth factor-1 in the rat. *Endocrinology* **120,** 491–496.

Hassing, J. M., Kletter, G. B., I'Anson, H., Wood, R. I., Beitins, I. Z., Foster, D. L. & Padmanabhan, V. (1993). Pulsatile administration of gonadotropin-releasing hormone does not alter the follicle-stimulating hormone (FSH) isoform distribution pattern of pituitary or circulating FSH in nutritionally growth-restricted ovariectomized lambs. *Endocrinology* **132,** 1527–1536.

Helliwell, R. J. A., Adam, C. L., Hannah, L. T., Kyle, C. E. & Williams, L. M. (1991). The distribution of central 2-[^{125}I]-iodomelatonin binding sites in the adult and foetal deer. *Journal of Reproduction and Fertility Abstract Series* no. 8, Abstr. 117.

Helliwell, R. J. A., Wallace, J. M., Aitken, R. P. & Robinson, J. J. (1992). Prenatal photoperiod times the onset of puberty in ewe lambs. *Journal of Reproduction and Fertility Abstract Series* no. 10, Abstr. 71.

Helliwell, R. J. A. & Williams, L. M. (1991). The development of melatonin binding sites in the ovine foetus. *Journal of Neuroendocrinology* **52,** Suppl. 1, 100.

Herbosa, C. G. & Foster, D. L. (1992). Prenatal photoperiod and the timing of puberty in the female lamb. *Biology of Reproduction* **46,** Suppl. 1, 60 Abstr.

Hileman, S. M., Schillo, K. K., Estienne, M. J., Hall, J. B., Green, M. A. & Boling, J. A. (1990). Effects of short-term intracerebroventricular (IVC) administration of insulin (INS) on LH release in lambs during restricted and *ad libitum* feeding. *Biology of Reproduction* **42,** Suppl. 1, 169 Abstr.

Hiney, J. K., Ojeda, S. R. & Dees, W. L. (1991). Insulin-like growth factor 1: a possible metabolic signal involved in the regulation of female puberty. *Neuroendocrinology* **54,** 420–423.

I'Anson, H., Foster, D. L., Foxcroft, G. R. & Booth, P. J. (1991). Nutrition and reproduction. In *Oxford Reviews of Reproductive Biology,* vol. 13, pp. 239–311 [S. R. Milligan, editor]. London: Oxford University Press.

I'Anson, H., Herbosa, C. G., Ebling, F. J. P., Wood, R. I., Bucholtz, D. C., Mieher, C. D., Foster, D. L. & Padmanabhan, V. (1993). Hypothalamic versus pituitary stimulation of luteinizing hormone secretion in the prepubertal female lamb. *Neuroendocrinology* **57,** 467–475.

Jansen, H. T., Khalid, M. & Jackson, G. L. (1991). N-methyl-D,L-aspartate induces a transient increase in LH secretion in the seasonally anestrous ewe. *Domestic Animal Endocrinology* **8,** 55–62.

Keane, M. G. (1974). Effect of bodyweight on attainment of puberty and reproductive performance in Suffolk × ewe lambs. *Irish Journal of Agricultural Research* **13,** 263–274.

Kennaway, D. J., Peek, J. C., Gilmore, T. A. & Royles, P. (1986). Pituitary response to LHRH, LH pulsatility and plasma melatonin and prolactin changes in ewe lambs treated with melatonin implants to delay puberty. *Journal of Reproduction and Fertility* **78,** 137–148.

Landefeld, T. D., Ebling, F. J. P., Suttie, J. M., Vannerson, L. A., Padmanabhan, V., Beitins, I. Z. & Foster, D. L. (1989). Metabolic interfaces between growth and reproduction. II. Characterization of changes in messenger ribonucleic acid concentrations of gonadotropin subunits, growth hormone and prolactin in nutritionally growth-limited lambs and the differential effects of increased nutrition. *Endocrinology* **125,** 351–356.

Lee, T. M., Smale, L., Zucker, I. & Dark, J. (1987). Influence of daylength experienced by dams on postnatal development of young meadow voles (*Microtus pennsylvanicus*). *Journal of Reproduction and Fertility* **81**, 337–342.

Lincoln, G. A., Ebling, F. J. P. & Martin, G. B. (1987). Endogenous opioid control of pulsatile LH secretion in rams: modulation by photoperiod and gonadal steroids. *Journal of Endocrinology* **115**, 425–438.

Lincoln, G. A. & Wu, F. C. W. (1991) Luteinizing hormone responses to N-methyl-D,L-aspartate during a photoperiodically-induced reproductive cycle in the ram. *Journal of Neuroendocrinology* **3**, 309–317.

McShane, T. M. & Keisler, D. H. (1991). Effects of dietary energy on ovarian function, estrogen suppression of luteinizing hormone and follicle-stimulating hormone, and competency of the gonadotropin surge. *Biology of Reproduction* **45**, 486–492.

Malven, P. V. (1986). Inhibition of pituitary LH release resulting from endogenous opioid peptides. *Domestic Animal Endocrinology* **3**, 135–144.

Meyer, S. L. & Goodman, R. L. (1986). Separate neural systems mediate the steroid-dependent and steroid-independent suppression of tonic luteinizing hormone secretion in the anoestrous ewe. *Biology of Reproduction* **35**, 562–571.

Mondragon, A. M., Gaverick, H. A., Mollett, T. A. & Elmore, R. G. (1986). Effect of serotonin on LH secretion patterns in ovariectomized cows. *Domestic Animal Endocrinology* **3**, 145–152.

Moore, R. W., Bass, J. J., Winn, G. W. & Hockey, H.-U. P. (1985). Relationship between carcass composition and first oestrus in Romney ewe lambs. *Journal of Reproduction and Fertility* **74**, 433–438.

Morgan, P. J., Barrett, P., Davidson, G. & Lawson, W. (1992). Melatonin regulates the synthesis and secretion of several proteins by pars tuberalis cells of the ovine pituitary. *Journal of Neuroendocrinology* **4**, 557–563.

Morgan, P. J., King, T. P., Lawson, W., Slater, D. & Davidson, G. (1991). Ultrastructure of melatonin responsive cells in the ovine pars tuberalis. *Cell Tissue Research* **263**, 529–534.

Morgan, P. J. & Williams, L. M. (1989). Central melatonin receptors: implications for a mode of action. *Experientia* **45**, 955–965.

Nicholls, T. J., Follet, B. K., Goldsmith, A. R. & Pearson, H. (1988). Possible homologies between photorefractoriness in sheep and birds: the effect of thyroidectomy on the length of the ewe's breeding season. *Reproduction Nutrition Développement* **28**, 375–385.

Nowak, R. & Rodway, R. G. (1985). Effect of intravaginal implants of melatonin on the onset of ovarian activity in adult and prepubertal ewes. *Journal of Reproduction and Fertility* **74**, 287–293.

Ogilvy, A. L. & Shalet, S. M. (1992). Growth hormone and puberty. *Journal of Endocrinology* **135**, 405–406.

Padmanabhan, V., Ebling, F. J. P., Sonstein, J., Fenner, D. E., Kelch, R. P., Foster, D. L. & Beitins, I. Z. (1989). Bioactive follicle-stimulating hormone release in nutritionally growth-retarded ovariectomized lambs: regulation by nutritional repletion. *Endocrinology* **125**, 2517–2526.

Padmanabhan, V., Mieher, C. D., Borondy, M., I'Anson, H., Wood, R. I., Landefeld, T. D., Foster, D. L. & Bietins, I. Z. (1992). Circulating bioactive follicle-stimulating hormone and less acidic follicle-stimulating hormone isoforms increase during experimental induction of puberty in the female lamb. *Endocrinology* **131**, 1131–1138.

Paterson, A. M., Martin, G. B., Foldes, A., Maxwell, C. A. & Pearce, G. P. (1992). Concentrations of plasma melatonin and luteinizing hormone in domestic gilts reared under artificial long or short days. *Journal of Reproduction and Fertility* **94**, 85–95.

Rawlings, N. C. & Churchill, I. J. (1990). Effect of naloxone on gonadotrophin secretion at various stages of development in the ewe lamb. *Journal of Reproduction and Fertility* **89**, 503–509.

Recabarren, S. E., Zapata, P. & Parilo, J. (1990). Disappearance of opioidergic tone on LH secretion in underfed prepubertal sheep. *Hormone and Metabolic Research* **22**, 225–228.

Reiter, R. J. (1991). Pineal melatonin: cell biology of its synthesis and of its physiological interactions. *Endocrine Reviews* **12**, 151–180.

Reyes, A., Luckhaus, J. & Ferin, M. (1991). Unexpected inhibitory action of N-methyl-D,L-aspartate on luteinizing hormone release in adult ovariectomized rhesus monkeys: a role of the hypothalamic–adrenal axis. *Endocrinology* **127**, 724–729.

Robinson, J. J. (1990). Nutrition in the reproduction of farm animals. *Nutrition Research Reviews* **3**, 253–276.

Rodriguez, R. E., Benson, B., Dunn, A. M. & Wise, M. E. (1993). Age-related changes in biogenic amines, opiate, and steroid receptors in the prepubertal bull calf. *Biology of Reproduction* **48**, 371–376.

Rodway, R. G., Swift, A. D., Nowak, R., Smith, J. A. & Padwick, D. (1985). Plasma concentrations of melatonin and the onset of puberty in female lambs. *Animal Reproduction Science* **8**, 241–246.

Schillo, K. K., Hall, J. B. & Hileman, S. M. (1992). Effects of nutrition and season on the onset of puberty in the beef heifer. *Journal of Animal Science* **70**, 3994–4005.

Schreihofer, D. A., Amico, J. A. & Cameron, J. L. (1993a). Reversal of fasting-induced suppression of luteinizing hormone (LH) secretion in male rhesus monkeys by intragastric nutrient infusion: evidence for rapid stimulation of LH by nutritional signals. *Endocrinology* **132**, 1890–1897.

Schreihofer, D. A., Parfitt, D. B. & Cameron, J. L. (1993b). Suppression of luteinizing hormone secretion during short-term fasting in male rhesus monkeys: the role of metabolic *versus* stress signals. *Endocrinology* **132**, 1881–1889.

Serrón-Ferré, M., Vergara, M., Parraguez, V. H., Riquelme, R. & Llanos, A. J. (1989). Fetal prolactin levels respond to a maternal melatonin implant. *Endocrinology* **125**, 400–403.

Shi, Z. D. & Barrell, G. K. (1992). Requirement of thyroid function for the expression of seasonal reproductive and related changes in red deer (*Cervus elaphus*) stags. *Journal of Reproduction and Fertility* **94**, 251–259.

Sisk, C. L. & Bronson, F. H. (1986). Effects of food restriction and restoration of gonadotropin and growth hormone secretion in immature male rats. *Biology of Reproduction* **35**, 554–561.

Skinner, D. C., Goode, J. & Robinson, J. E. (1993). Does melatonin influence the luteinizing hormone releasing hormone (LHRH)-stimulated secretion of luteinizing hormone from the foetal ovine pars tuberalis (PT) and pars distalis (PD) *in vitro*? *Journal of Reproduction and Fertility Abstract Series* no. 11, Abstr. 28.

Steiner, R. A. (1987). Nutritional and metabolic factors in the regulation of reproductive hormone secretion in the primate. *Proceedings of the Nutrition Society* **46**, 159–175.

Stetson, M. H., Elliott, J. A. & Goldman, B. D. (1986). Maternal transfer of photoperiodic information influences the photoperiodic response of prepubertal Djungarian hamsters (*Phodopus sungorus sungorus*). *Biology of Reproduction* **34**, 664–669.

Sunderland, S. J., O'Callaghan, D., Boland, M. P. & Roche, J. F. (1990). The effect of pre- and postnatal photoperiod on the onset of puberty in ewe lambs. *Journal of Reproduction and Fertility Abstract Series* no. 6, Abstr. 42.

Suttie, J. M., Fennessy, P. F., Corson, I. D., Laas, F. J., Crosbie, S. F., Butler, J. H. & Gluckman, P. D. (1989). Pulsatile growth hormone, insulin-like growth factors and antler development in red deer (*Cervus elaphus scoticus*) stags. *Journal of Endocrinology* **121**, 351–360.

Suttie, J. M., Foster, D. L., Veenvliet, B. A., Manley, T. R. & Corson, I. D. (1991a). Influence of food intake but independence of body weight on puberty in female sheep. *Journal of Reproduction and Fertility* **92**, 33–39.

Suttie, J. M., Kostyo, J. L., Ebling, F. J. P., Wood, R. I., Bucholtz, D. C., Skottner, A., Adel, T. E., Towns, R. J. & Foster, D. L. (1991b). Metabolic interfaces between growth and reproduction. IV. Chronic pulsatile administration of growth hormone and the timing of puberty in the female sheep. *Endocrinology* **129**, 2024–2032.

Suttie, J. M., White, R. G., Breier, B. H. & Gluckman, P. D. (1991c). Photoperiod associated changes in insulin-like growth factor-1 in reindeer. *Endocrinology* **129**, 679–682.

Terasawa, E., Krook, C., Hei, D. L., Gearing, M., Schultz, N. J. & Davis, G. A. (1988). Norepinephrine is a possible neurotransmitter stimulating pulsatile release of luteinizing hormone releasing hormone in the rhesus monkey. *Endocrinology* **123**, 1808–1816.

Thiéry, J. C. & Martin, G. B. (1991). Neurophysiological control of the secretion of gonadotrophin-releasing hormone and luteinizing hormone in the sheep – a review. *Reproduction, Fertility and Development* **3**, 137–173.

Vriend, J., Sheppard, M. S. & Balo, R. M. (1988). Melatonin increases serum insulin-like growth factor-1 in male Syrian hamsters. *Endocrinology* **122**, 2558–2561.

Webster, J. R. & Barrell, G. K. (1985). Advancement of reproductive activity, seasonal reduction in prolactin secretion and seasonal pelage changes in pubertal red deer hinds (*Cervus elaphus*) subjected to artificially shortened daily photoperiod or daily melatonin treatments. *Journal of Reproduction and Fertility* **73**, 255–260.

Webster, J. R., Moenter, S. M., Woodfill, C. J. I. & Karsch, F. J. (1991). Role of the thyroid gland in seasonal reproduction. II. Thyroxine allows a season-specific suppression of gonadotropin secretion in sheep. *Endocrinology* **129**, 176–183.

Wolfe, M. W., Robertson, M. S., Stumpf, T. T., Kittok, R. J. & Kinder, J. E. (1992). Modulation of luteinizing hormone and follicle-stimulating hormone in circulation by interactions between endogenous opioids and oestradiol during the peripubertal period of heifers. *Journal of Reproduction and Fertility* **96**, 165–174.

Wood, R. I., Ebling, F. J. P., I'Anson, H., Bucholtz, D. C., Yellon, S. M. & Foster, D. L. (1991*a*). Prenatal androgens time neuroendocrine sexual maturation. *Endocrinology* **128**, 2457–2468.

Wood, R. I., Ebling, F. J. P., I'Anson, H. & Foster, D. L. (1991*b*). The timing of neuroendocrine sexual maturity in the male lamb by photoperiod. *Biology of Reproduction* **45**, 82–88.

Yellon, S. M. & Foster, D. L. (1985). Alternate photoperiods time puberty in the female lamb. *Endocrinology* **116**, 2090–2097.

Yellon, S. M. & Foster, D. L. (1986). Melatonin rhythms time photoperiod induced puberty in the female lamb. *Endocrinology* **119**, 44–49.

Yellon, S. M. & Longo, L. D. (1987). Melatonin rhythms in fetal and maternal circulation during pregnancy in sheep. *American Journal of Physiology* **252**, E799–E802.

Yellon, S. M. & Longo, L. D. (1988). Effect of maternal pinealectomy and reverse photoperiod on the circadian melatonin rhythm in the sheep and fetus during the last trimester of pregnancy. *Biology of Reproduction* **39**, 1093–1099.

Zemdegs, I. Z., McMillen, I. C., Walker, D. W., Thorburn, G. D. & Nowak, R. (1988). Diurnal rhythms in plasma melatonin concentrations in the fetal sheep and pregnant ewe during late gestation. *Endocrinology* **123**, 284–289.

Printed in Great Britain