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Estradiol feedback on gonadotropin secretion during the transition to adulthood in the bovine

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ESTRADIOL FEEDBACK ON GONADOTROPIN SECRETION DURING THE TRANSITION TO ADULTHOOD IN THE BOVINE

by

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A DISSERTATION

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GRADUATE COLLEGE
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ESTRADIOL FEEDBACK ON GONADOTROPIN SECRETION DURING THE TRANSITION TO ADULTHOOD IN THE BOVINE

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Regulation of LH and FSH secretion by estradiol was evaluated during sexual development in the bovine. Involvement of opioid neuropeptides in modulating estradiol inhibition of gonadotropin secretion during puberty in heifers was investigated in the first two experiments. Low levels of estradiol inhibited gonadotropin secretion in prepubertal ovariectomized heifers. Administration of the opioid antagonist, naloxone, blocked the inhibitory effects of estradiol and caused an increase in LH secretion. Naloxone had no effect on gonadotropin secretion in prepubertal heifers that were ovariectomized and not administered estradiol. As heifers matured, estradiol inhibition of gonadotropin secretion waned as did the ability of naloxone to disinhibit LH secretion in ovariectomized heifers treated with estradiol. By the time control heifers had attained puberty, estradiol no longer inhibited gonadotropin secretion and opioids had only minor inhibitory effects on LH secretion in ovariectomized heifers administered estradiol.

Estradiol feedback on gonadotropin secretion in bovine males during the time of the peripubertal change in estradiol feedback in bovine females was examined in the second experiment. Administration of low levels of estradiol

inhibited LH and FSH secretion in gonadectomized bovine males and females. Inhibition occurred during the time intact heifers were prepuberty. During the time estradiol inhibition of gonadotropin secretion was abating in females, a simultaneous decline was observed in males. Moreover, at the end of the study, estradiol increased tonic LH secretion in gonadectomized males and females above concentrations detected in gonadectomized animals not receiving estradiol. This was at a time when intact heifers had initiated estrous cycles.

The final experiment investigated estradiol feedback on gonadotropin secretion in adult gonadectomized males and females administered various physiological concentrations of estradiol. Administration of low concentrations of estradiol increased mean concentrations of LH and amplitude of LH pulses in both sexes and increased mean concentrations of FSH in males, but did not alter FSH in females compared to administration of sham implants. High physiological concentrations of estradiol suppressed LH and FSH secretion in bovine males and females.

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I have learned a lot and matured considerably over the

past six years. The changes that I have gone through bring to mind a Zen epigram quoted by Dr. Ernie Knobil as an analogy of how our understanding of science changes:

> To a man who knows nothing, Mountains
> are Mountains, Water is Water and
> Trees are Trees.
>
> When he has learned a little, Mountains
> are no longer Mountains, Water is no
> longer Water and Trees are no longer Trees.
>
> But when he has fully understood,
> Mountains are again Mountains, Water is
> Water and Trees are again Trees.

My challenge as a scientist is to constantly strive to progress from the middle to the last stanza.

Michael Wolfe

DEDICATION

This dissertation is dedicated to my wife, Patricia, and our daughter, Malissa. God has truly blessed me with wonderful companions.

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LITERATURE REVIEW

I. Introduction

Puberty is a maturational state that has many diverse definitions. Puberty in females is commonly defined as the occurrence of the first estrus associated with ovulation (Wiltbank et al., 1966). The occurrence of the first behavorial estrus followed by the formation of a corpus luteum that persists for a period of time that is normal for a particular species is a more precise definition. Regardless of definition, puberty in beef cattle is clearly an important physiological state a heifer must attain if reproduction is to ensue. The time when puberty occurs is a crucial component of economic success in the beef cattle industry.

Early attainment of puberty is important in cattle. In management systems that are designed to have heifers give birth to calves at two years of age, heifers must be pregnant by 15 months of age. Thus, the heifers must attain puberty before 15 months of age for conception to occur at this time. Not all heifers reach puberty by 15 months of age. Dow et al. (1982) reported that the percentage of heifers that reached puberty by 15 months varied greatly across breeds, ranging from 38% for straightbred Herefords to 92% for Hereford x Red Poll crossbred heifers. Heifers that conceive after they reach 15 months of age will give birth to calves later in the year and will wean a younger, lighter calf if all calves are weaned at the same time.

An advanced age at puberty and the resulting delay in conception can adversely affect the performance of a heifer's first calf and furthermore, this may have a detrimental influence on the heifer's lifetime production (Pinney et al., 1972; Lesmeister et al., 1973). Post (1984) reported that Zebu x British crossbred heifers that reached puberty at earlier ages, had fewer matings in which conception failed and shorter postpartum periods of anestrus in subsequent years. Therefore, the time when a heifer reaches puberty not only affects her reproductive capabilities as a heifer, but also her future reproductive performance and lifetime productivity.

Genetic relationships of age at puberty and other reproductive traits have been reported in cattle and other species. Favorable genetic correlations between testis size (circumference) and age at puberty (Brinks et al., 1978) or age at first conception (Toelle and Robinson, 1985) have been estimated from half-sib and sire-daughter analyses. Testis size has, in turn, been shown to be genetically related in a favorable manner to pregnancy rate in cows (Toelle and Robinson, 1985), onset of the breeding season in ewes (Land, 1978) and ovulation rate in sheep (Land, 1973; Land and Carr, 1975), mice (Land, 1973; Islam et al., 1975; Joakimsen and Baker, 1977; Eisen and Johnson, 1981) and swine (Proud et al., 1976; Schinckel et al., 1983). The genetic relationships of age at puberty with other important reproductive traits have not been estimated for cattle. The correlation of age at

puberty in heifers and other reproductive traits (pregnancy rate, etc.) in cows to testis size in bulls presents the possibility that selection for early puberty could be beneficial to reproductive efficiency of the cow herd. The genetic relationship of age at puberty to reproductive performance requires investigation to determine if benefits could be realized from genetic selection for age at puberty.

The influence of early age at puberty on reproductive efficiency and productivity of cattle indicates its importance in cattle production. However, the endocrine mechanisms that control attainment of puberty are poorly understood in both the bovine male and female. Due to the correlations between age at puberty in heifers and testis size in bulls, it is important to understand the similarities and differences between sexes in endocrine control of puberty and subsequent reproductive function. A better understanding of the mechanisms regulating puberty in the bovine may lead to future management practices that substantially improve the reproductive performance and overall productivity of the bovine.

II. Prepuberty

A. Gonadotropin Secretory Profiles

In order to better understand the mechanisms involved in regulating the onset of puberty, it is first necessary to examine the changes that occur in the endogenous pattern of secretion of hormones involved in reproduction. Fluctuations in the pattern of release of these hormones provide insights into the time periods when major changes occur. Furthermore, these observations may provide valuable information as to which components of the hypothalamo-hypophyseal-gonadal axis are functional or nonfunctional. Data obtained from longitudinal studies of hormone profiles lay the foundation for future scientific endeavors into the study of puberty and reproduction.

Rat

Postnatal development from birth to puberty in the female rat has been divided into four phases: a neonatal period (birth to d 7; birth = d 0), an infantile period (d 8 to d 21), a prepubertal period (d 22 to 30) and a peripubertal period which is highlighted by the occurrence of first ovulation (Ojeda et al., 1986). Secretion of LH is initiated during the neonatal period (d 2) but remains low, while secretion of FSH increases during this period (Ojeda et al., 1986). Serum FSH concentrations continue to increase during infancy, peak on d 12 to d 15 and then decline in female rats (Ojeda and Ramirez, 1972). Little change is observed in secretion of LH. This

quiescence continues through much of the prepubertal period. Pituitary content of LH peaks on d 20 while FSH peaks on d 30 in the rat.

Major changes in secretion occur during the transition from the prepubertal to the peripubertal period. A diurnal pattern of LH secretion begins to be established with increases in LH pulse amplitude observed during the afternoon (Andrews and Ojeda, 1981; Urbanski and Ojeda, 1985). Ovarian production of estradiol is increased (Ojeda et al., 1976), possibly due to increased ovarian stimulation by gonadotropins. An overall increase in secretion of LH, FSH and estradiol has been observed during the peripubertal period, culminating in the gonadotropin surge and first ovulation (Docke et al., 1984c; Taya and Sasamoto, 1988). Thus, a series of secretory changes occur in the female rat prior to the time of puberty.

Secretory changes are also observed during sexual development in the male rat, however, they have not been characterized as extensively as those in the female. Secretion of LH and FSH increases during the first 2 hr following birth in males and then declines to levels observed 2 d prior to birth (Corbier et al., 1978). Ojeda and Ramirez (1972) observed that secretion of LH was similar between male and female rats from 5 to 45 d of age. In contrast, FSH differed between sexes in that no change occurred during this time in males, while secretion of FSH increased from 5 to 15 d of age in females. In a more extensive study, Lee et al. (1975) observed an increase in LH secretion from d 6 to 14 of life,

followed by a decline through d 30. Thereafter, secretion of LH rose and was paralleled by an increase in testosterone. Secretion of FSH followed a different pattern. Serum FSH declined from birth to d 6 and fluctuated at low levels until increasing again between d 30 to 45. The study conducted by Lee et al. (1975) indicates that gonadotropin secretion increases during the days prior to puberty in the male which is similar to observations in the female.

Primate

Winter et al. (1975) examined the secretory profile of LH and FSH in boys and girls from 5 d to 4 yr of age. Secretion of LH was similar between boys and girls with secretion peaking at 1 mo of age and then declining (4 mo) and remaining low during the remainder of the study. Secretion of FSH differed between sexes. Serum FSH peaked at 3 mo of age in both boys and girls, but peaked at higher concentrations in girls. Furthermore, secretion had declined in boys by the time they were 4 mo of age, but remained elevated in girls with a gradual decline occurred until 4 yr of age. A similar pattern of secretion was observed in the female chimpanzee (Winter et al., 1975). Studies conducted closer to the time of puberty in boys and girls have revealed increases in secretion of LH, FSH, estradiol, testosterone and inhibin as sexual development advanced (Penney et al., 1977; Burger et al., 1988).

A similar increase in secretion of LH during sexual maturation was observed in female Rhesus monkeys (Terasawa et

al., 1984). Serum LH concentrations were low, with no circadian fluctuation in young monkeys (prepubertal). As monkeys matured, LH secretion increased and circadian rythmns were established (early pubertal). Secretion of LH continued to increase from first menarche (mid pubertal) to time of first ovulation (late pubertal). This increase in LH secretion during sexual development was much more dramatic in the evening than during the morning, similar to the rat (Urbanski and Ojeda, 1985). Furthermore, the increase in LH secretion (maturational and circadian) during pubertal development has been associated with an increase in LHRH secretion (Watanabe and Terasawa, 1989). Mean concentration of LHRH, determined by push-pull perfusion, increased from 0.70 pg/ml at 15.7 mo of age (prepuberty) to 2.41 pg/ml at 26.1 mo of age (early puberty; prior to menarche) and 8.33 pg/ml at 40 mo of age (midpuberty; after menarche, but before first ovulation). Thus, the increase in LH secretion prior to puberty is due to an increase in hypothalamic stimulation.

Sheep

Both LH and FSH have been detected in fetal lambs. Plasma concentrations of LH and FSH peaked during mid gestation and then declined as time of parturition neared (Foster et al., 1972b). Pituitary content of both LH and FSH continued to increase until the time of parturition. Subsequent to parturition, pituitary content of LH declined, but had begun to increase again by postnatal d 18.

An increase in secretion of LH has also been observed in

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