INTRODUCTION

Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secreted by the anterior pituitary are important regulators of male and female reproductive processes. The hypothalamic hormone luteinizing hormone releasing hormone (LHRH) has been shown to regulate the release of LH and FSH from the anterior pituitary (Schally et al., 1971). Extensive work has been done on the interaction between gonadal steroids, hypothalamic LHRH and the anterior pituitary in the synthesis and release of LH and this topic has been reviewed by Kalra and Kalra (1983). The regulation of the secretion of FSH, however, cannot be explained adequately with LHRH as the sole regulatory hypothalamic hormone; this is due to a significant divergence between FSH and LH secretion during the ovulatory cycle (Bast and Greenwald, 1974; Smith et al., 1975), after ovariectomy in the rat (Mahesh et al., 1972; Tapper et al., 1972; Zanisi and Martini, 1975a) and during puberty (Dohler and Wuttke, 1975; Payne et al., 1977). This chapter will review the current concepts concerning the role of (a) specific FSH releasing and inhibiting peptides, (b) neuroendocrine control of FSH secretion and (c) steroid hormones in the divergent secretion of FSH and LH.

SPECIFIC FSH RELEASING AND INHIBITING PEPTIDES

The most direct way to explain divergent secretion of FSH and LH under selected physiological conditions would be to postulate the presence of a distinct FSH releasing factor (FSH-RF). Such a postulate was made repeatedly (Bowers et al., 1973; Igarashi et al., 1973; Igarashi and McCann, 1974) but has not been supported adequately by experimental evidence (Shahmanesh and Jeffcoate, 1976; Schally et al., 1976). More recently, the concept of a FSH-RF is being revived by using a combination of bioassays and radioimmunoassays (Lundanes et al., 1980; Mizunuma et al., 1983). Nevertheless the presence of a specific FSH-RF is still not widely accepted.

The concept of a gonadal peptide responsible for the modulation of FSH secretion was first proposed by McCullagh in 1932. Extensive work on the presence of such a peptide of ovarian origin has been carried out by several investigators (Schwartz and Channing, 1977; Rush et al., 1981) and cyclic fluctuations of inhibin-like material has been reported in ovarian tissue and ovarian venous blood (Chappel, 1979; DePaolo et al., 1979). The ovarian peptides have now been isolated and characterized (Ling et al., 1985; Mason et al., 1985; Miyamoto et al., 1985; Rivier et al., 1985;
Robertson et al., 1985, 1986). Porcine inhibin occurs as two heterodimers with a common α-subunit and a different but related β-subunit. An infusion of antibodies to inhibin on the day of proestrus and estrus in the rat enhanced the magnitude of FSH secretion without altering LH (Rivier et al., 1986). However it did not alter the pattern and duration of FSH elevation indicating the existence of other controlling mechanisms for FSH release in addition to inhibin. The β-subunit of inhibin has been found to have FSH releasing activity (Ling et al., 1986; Vale et al., 1986) and requires a period of 4 to 24 h to manifest its biological activity. Further evaluation is needed to determine if this peptide plays a physiological role in the regulation of FSH secretion.

NEUROENDOCRINE CONTROL OF FSH SECRETION

It is well recognized that electrical stimulation of the preoptic suprachiasmatic nuclear region of the hypothalamus on the day of proestrus brings about a proestrus type of LH and FSH surge. Electrical stimulation of the dorsal anterior hypothalamic area (DAHA) elicits preferential FSH release (Kalra et al., 1971; Chappel and Barracough, 1976). Bilateral lesions of the DAHA resulted in a reduction of serum FSH levels during proestrus (Lumpkin and McCann, 1982). Selective release of FSH was also shown to occur after prostaglandin E2 was implanted stereotaxically in the DAHA region (Ojeda et al., 1972). These observations indicate the presence of separate neural pathways involved in the control of FSH and LH and anatomical evidence for these pathways was provided by Kimura and Kawakami (1978). Further work by several investigators has shown that deafferentation of neurosecretory cells in the arcuate-median eminence region from those in the preoptic-anterior hypothalamic area prior to 1800 h of proestrus reduced or abolished the FSH release on estrus but deafferentation after 1800 h did not have any effect (Chappel et al., 1979; Rush et al., 1980, 1982; Blake et al., 1982). The absence of the requirement for LHRH in the secretion of FSH on estrus was further confirmed by demonstrating that antibodies to LHRH administered on the day of estrus did not have any effect on FSH secretion (Hasegawa et al., 1981; Rush et al., 1982). Blockade of the proestrus surge of FSH and LH by the administration of phenobarbital also resulted in the abolition of the elevated secretion of FSH at estrus. Experiments with deafferentation before 1800 h and phenobarbital blockade of the surge suggest that FSH and LH secretion at proestrus may be essential for the secretion of FSH on estrus. Several investigators have studied the effect of LH and FSH administration on subsequent secretion and release of FSH (Ojeda and Ramirez, 1969, 1970; Schwartz and Talley, 1978; Ashiru and Blake, 1979, 1980; Ashiru et al., 1981; Coutifaris and Chappel, 1982). Both hormones were able to stimulate FSH release by the anterior pituitary. Binding sites for FSH in the hypothalamus have also been reported (Davies et al., 1975).

It is now well established that the secretion of LHRH by the hypothalamus is pulsatile in nature and this pulsatility is essential for maintaining the sensitivity of the anterior pituitary to LHRH (Belchetz et al., 1978). The mode of administration of LHRH (Pickering and Fink, 1977; Wise et al., 1979; Turgeon and Waring, 1982) or the pulse intervals (Lincoln, 1979; Wildt et al., 1981; Pohl et al., 1983) has been shown to induce a divergence in FSH and LH secretory patterns.

REGULATION OF FSH AND LH SECRETION BY ESTROGENS: EVIDENCE OF DIFFERENTIAL REGULATION IN THE ABSENCE OF GONADAL PEPTIDES

Estrogens exert both a positive and a negative feedback effect on gonadotropin secretion. The presence of the negative feedback system was established by classical experiments demonstrating that ovariectomy