

In terms of percentage of the basal value, LH increment was more in the pre-pubertal (54 fold) than seen in the adults (32 fold), whereas the FSH increment was just opposite, being 2.5 fold for the pre-pubertal and 4.2 fold for the mature animals. Prior treatment of the animals with sex steroids and gonadotropins upset the steroid-gonadotropin feed-

back mechanism, and great divergence emerged between immature and mature animals when LH-RH was infused in them. The significance of this difference in the observed response during mammalian sexual maturation is discussed.

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### Hypothalamic-Pituitary-Ovarian Feedback Mechanisms

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Feedback control involves regulation predominantly by circulating levels of hormones. There are stimulatory and inhibitory as well as internal and external forms of feedback. In the classic external feedback the controlling signals are the hormones produced by the peripheral target glands. The receptors which respond to changes in circulating steroid levels by initiating a change in the secretion of gonadotropins are located in the basal medial hypothalamus, anterior hypothalamus and preoptic area as well as the anterior pituitary. The stimulatory effects of gonadal steroids which are thought to bring about ovulation in the normal animal are presumably mediated in the suprachiasmatic region and preoptic area. It is postulated that a noradrenergic synapse mediates the stimulatory effects of estrogen and progesterone on the ovulatory release of gonadotropins (cyclic release center). The arcuate nucleus-median eminence dopaminergic tract may be involved in the so-called tonic discharge of gonadotropins and in the negative feedback action of gonadal steroids.

Sex steroids also affect the response to natural and synthetic LRH. Complex interaction of sex steroids both in the hypothalamus and pituitary may evoke differential release of LH and FSH thus indicating the possible existence of separate control mechanisms for LH and FSH.

There is recent evidence for short feedback loops, also referred to as auto or internal feedback. Short systems are involved in the regulation of LH and FSH secretion. LH *via* an effect on the basal median eminence seems to inhibit its own secretion.

Inhibitory as well as stimulatory short feedback mechanisms have been described for the control of FSH secretion. This positive short feedback appears to be peculiar for immature animals and may play a role at the time of puberty.

Finally, a third type described as ultrashort feedback has been found for the control of the gonadotropin releasing hormone on its own production. There are data indicating that hypothalamic LRH content is increased following small doses of chronically applied synthetic LRH in rodents under conditions which do not alter circulating gonadotropins or pituitary sensitivity to LRH.

Control systems concepts have become widespread among reproductive neuro-endocrinologists. No sufficiently reliable data exist today which could be used to successfully apply the systems analysis approach.

### Identification and Measurement of LH-RH in Biological Fluids by Radioimmunoassay

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A radioimmunoassay for LH-RH has been developed using the following reagents: Synthetic LH-RH decapeptide (Hoechst) as standard; an antiserum raised in a rat to the des-glu<sup>1</sup>, his<sup>2</sup>-octapeptide of LH-RH conjugated to albumin; [<sup>125</sup>I]labelled

LH-RH decapeptide; ethanol precipitation is used to separate free and bound fractions.

The assay is highly specific for LH-RH and particularly for the C-terminus of the molecule; lack of the C-terminal amide group results in a complete loss of immunoreactivity. The sensitivity of the assay is 0.5 pg of LH-RH.

Assay of *hypothalamic extracts* after gel filtration, thin-layer chromatography and ion-exchange chromatography has shown that synthetic LH-RH and mammalian and avian LH-RH are immunologically and chromatographically identical.



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