

LH-RH can also be assayed in *urine*. 1 – 2 percent of an injected dose is excreted within 8 hours. Basal excretion rates in normal human subjects are 15 – 60 ng/day. Urine LH-RH is immunochemically identical but chromatographically (on ion-exchange columns) different and evidence suggests that it is the des-glu<sup>1</sup>-nonapeptide or des-glu<sup>1</sup>, his<sup>2</sup>-octapeptide of LH-RH.

LH-RH has been detected and measured by radioimmunoassay in the *blood* of rats, rabbits, chickens,

sheep and human subjects. In man the levels in peripheral blood range between <0.25 pg/ml and 3.5 pg/ml. Levels of up to 10,000 pg/ml can be detected in the jugular vein of the ewe during the oestrous cycle. Ion-exchange chromatography of serum extracts from various species followed by radioimmunoassay suggests that circulating immunoreactive LH-RH is heterogeneous and 4 distinct components have been identified.

### LH-RH in Paediatrics

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Secretion of gonadotropins before puberty has been considered a dormant function until measurable levels in plasma and urine were reported in young children by means of radioimmunoassay techniques (Johanson *et al.* 1969, Raiti *et al.* 1969). More detailed studies and reports on feedback of sex hormones in prepuberal children (Burr *et al.* 1970, Kehl *et al.* 1973) supported the earlier concept of the gonadostat already functioning before puberty with decreasing sensitivity for circulating sex hormones. Even with expanding insight into the complicated dependency of CNS, pituitary, and end organ for the maturation of the reproductive system in man the mechanism of puberty onset remains obscure (Root 1973, Visser 1973).

The purification and synthesis of the hypothalamic gonadotropin releasing factor (LH-RH) (Schally *et al.* 1971, Monahan *et al.* 1971) provides a new tool for the evaluation of physiological and pathological relations between CNS and pituitary (Job *et al.* 1972, Grumbach *et al.* 1972). At present it is still uncertain whether the prepuberal pituitary can be stimulated to adult secretion of FSH and LH by LH-RH (Kastin *et al.* 1972). Dose responses of graded infusions of LH-RH in prepuberal boys and girls have not been reported so far. With a reliable RIA for FSH and LH in children (Joel *et al.* 1973)

we found a distinct rise of the gonadotropins in prepuberal boys but no dose response after LH-RH (Hoe 471) in doses of 6.25 – 200 µg/m<sup>2</sup>. In contrast prepuberal girls had a much higher rise of FSH with clear dose response while LH was comparable to boys. After puberty onset the starting levels of FSH were higher but were only moderately elevated after LH-RH with nearly no dose response. LH levels were less elevated at start but could be stimulated to a greater extent with more pronounced dose response. The interpretation of a sex dependent alteration in responsiveness and depletion of the pituitary during puberty will await more data on stimulation and feedback. Estrogens may play a role in prepuberal girls in triggering the more pronounced stimulation of FSH. The preponderance of LH after puberty onset may reflect the start of cyclic discharge and importance in adult females.

For the clinical evaluation of the CNS-pituitary axis in hypo- and hypergonadism in children first promising results have been published (Job *et al.* 1972, Roth *et al.* 1972). The group of constitutional delay of maturation can be clearly distinguished. Results for organical gonadotropin deficiency are more difficult to interpret (Grumbach 1972). In precocious puberty the LH-RH test may be useful for the diagnosis of true or pseudoprecocity but for the treatment with competitive LH-RH analogs also (Vale *et al.* 1972). Routine treatment which still is not entirely satisfactory would be another field of this test in paediatrics. (Literature on request.)

### LH-RH in Ovarian-Insufficiency \*

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The use of synthetic LH-RH permits the assessment of pituitary responsiveness and helps to differentiate

ovarian dysfunction originating in the pituitary from that originating in the hypothalamus and or in the central nervous system. In 100 patients with various types of ovarian insufficiency LH-RH-stimulation was done. The patients were classified according to their total gonadotrophin excretion: group 1: <2.4 IU II. IRP HMG/24 h, group 2:

\* Supported by DFG, Sonderforschungsbereich -34-, "Endokrinologie".

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