

# Contents

Preface . . . . .	9
Abbreviations used in the text. Conversion into SI units . . . . .	10
<b>1. Recent development in hypothalamic-hypophyseal regulation of ovarian function . . . . .</b>	<b>12</b>
Pulsatile LH and LH-RH release . . . . .	13
Permissive action of LH-RH . . . . .	17
Desensitization of the anterior lobe of the pituitary and "down regulation" . . . . .	20
Modulation of LH-RH action . . . . .	23
Models of cycle control . . . . .	23
References . . . . .	24
<b>2. Chemistry and biological effect of LH-RH and its analogues . . . . .</b>	<b>29</b>
Terminology . . . . .	29
Biological evidence of LH-RH . . . . .	29
Isolation, structure and synthesis of LH-RH . . . . .	30
Unity or dualism of LH-RH and FSH-RH . . . . .	31
International LH-RH standard . . . . .	32
Biological action of LH-RH . . . . .	32
Immunology of LH-RH . . . . .	36
Structure and functional relationship of LH-RH analogues . . . . .	38
Superactive LH-RH analogues . . . . .	40
Inhibitory LH-RH analogues . . . . .	44
References . . . . .	48
<b>3. Physiology of LH-RH . . . . .</b>	<b>56</b>
Sites of production, distribution and localization of LH-RH . . . . .	56
LH-RH biosynthesis . . . . .	62
LH-RH circulation . . . . .	63
LH-RH degradation . . . . .	64
References . . . . .	65

<b>4. Receptors for LH-RH. Mechanism of LH-RH action . . . . .</b>	<b>70</b>
Pituitary receptors . . . . .	70
Ovarian receptors . . . . .	75
Autoregulation of LH-RH receptors . . . . .	78
References . . . . .	82
<b>5. Factors affecting LH-RH and LH release . . . . .</b>	<b>88</b>
Effect of oestrogens . . . . .	88
Effect of progesterone . . . . .	91
Effect of neurotransmitters . . . . .	94
Effect of catecholamines . . . . .	94
Effect of serotonin . . . . .	100
Effect of acetylcholine . . . . .	101
Effect of $\gamma$ -aminobutyric acid (GABA) . . . . .	101
Effect of prostaglandins . . . . .	102
Effect of opioid peptides and opiates . . . . .	105
Effect of other factors . . . . .	109
References . . . . .	110
<b>6. LH-RH under physiological conditions . . . . .</b>	<b>120</b>
Methods of biological and RIA assessment of LH-RH . . . . .	120
LH-RH during oestrous and menstrual cycle . . . . .	120
LH-RH during puberty . . . . .	124
LH-RH after castration and menopause . . . . .	126
LH-RH during pregnancy, puerperium and lactation . . . . .	128
References . . . . .	131
<b>7. Effect of sex steroids on gonadotropin release by LH-RH in animals.</b>	
<b>Reactivity of the anterior pituitary . . . . .</b>	<b>137</b>
Effect of oestrogens . . . . .	137
Effect of progesterone . . . . .	143
Effect of testosterone . . . . .	145
References . . . . .	146
<b>8. LH-RH action in women . . . . .</b>	<b>150</b>
Acute administration of LH-RH (bolus injection) . . . . .	150
Repeated administration of LH-RH . . . . .	158
Long-term infusions of LH-RH . . . . .	162
Intermittent administration of LH-RH . . . . .	167
References . . . . .	167

<b>9. Anterior pituitary responsiveness in women and steroid interaction . . . . .</b>	<b>171</b>
Changes during menstrual cycle . . . . .	171
Changes in postmenopausal women and in primary hypogonadal states . . . . .	173
Changes in hypogonadotropic states . . . . .	174
Changes during development . . . . .	174
Two pools of pituitary gonadotropin response . . . . .	177
Qualitative changes of LH release . . . . .	179
Effects of oestrogens and other steroids on pituitary responsiveness . . . . .	182
Effect of oestrogens . . . . .	182
Effect of testosterone . . . . .	188
Effect of progesterone . . . . .	189
Effect of contraceptive steroids . . . . .	191
References . . . . .	192
<b>10. Action of LH-RH analogues in women and subhuman primates . . . . .</b>	<b>198</b>
Action of superactive agonists . . . . .	198
Action of inhibitory antagonists . . . . .	205
References . . . . .	208
<b>11. Antifertile effects of LH-RH and its analogues . . . . .</b>	<b>212</b>
Effects of LH-RH and superactive analogues . . . . .	212
Effects of inhibitory analogues . . . . .	221
References . . . . .	224
<b>12. Contraceptive methods on the basis of LH-RH superactive agonists . . . . .</b>	<b>230</b>
Chronic administration of LH-RH superactive agonists . . . . .	230
Luteolysis . . . . .	233
Contraception in men . . . . .	236
References . . . . .	236
<b>13. Diagnostic use of LH-RH tests . . . . .</b>	<b>239</b>
Simple LH-RH test . . . . .	239
Double-stimulation test and infusion test . . . . .	242
Combined tests . . . . .	245
LH-RH test with a double response . . . . .	247
References . . . . .	248
<b>14. Induction of ovulation by LH-RH and its analogues in women. I. Chronic continual administration . . . . .</b>	<b>254</b>
Induction of ovulation by LH-RH . . . . .	254
Ovulation timing . . . . .	260

Induction of ovulation by superactive analogues . . . . .	261
References . . . . .	263
<b>15. Induction of ovulation by LH-RH in women. II. Pulsatile administration</b>	<b>266</b>
Induction of ovulation by i. v. route . . . . .	266
Controlled hyperstimulation for fertilization in vitro . . . . .	270
Other results and problems with pulsatile administration; s. c. route . . . . .	270
References . . . . .	277
<b>16. Future field of other clinical uses of LH-RH and its analogues . . . . .</b>	<b>281</b>
Activation of the pituitary-ovarian system in treatment . . . . .	281
Hypogonadotropic hypogonadism . . . . .	281
Delayed puberty . . . . .	283
Cryptorchidism . . . . .	285
Block of the pituitary-ovarian system in treatment . . . . .	286
Endometriosis . . . . .	289
Precocious puberty . . . . .	290
Breast cancer . . . . .	292
Prostate cancer . . . . .	293
Further indications for block therapy with superactive analogues and antagonists.	297
References . . . . .	298
Index . . . . .	307