Appendix III

MASTER

Prostaglandins and The Dual Endocrine Role of the Testis

The testis can now be considered a dual endocrine organ producing both androgens and prostaglandins. Elucidation of the mechanisms involved in the synthesis of prostaglandins and androgens has shown that both occur in testes and their rates increase with age and development of the testes and diminish after hypophysectomy.

Gonadotropins increase the synthesis of both groups of compounds, but prostaglandin synthesis only is diminished by adrenalectomy. Prostaglandins exert physiological effects on the testes, for example exogenous prostaglandins and endogenous prostaglandin-like material modulate the contractions of rabbit testes in vitro.

The significance of the role of prostaglandins in modulating testicular contractions, and various physiological consequences, have been demonstrated in various ways. The autorhythmic contractions of a testis in vitro cease after repeated rinses with a balanced saline solution and begin again when prostaglandins are added to the media. Contractions are induced in a quiescent testis placed in bathing media from a contracting testis, uterus or intestine. This response is not duplicated in an inactive testis by addition of acetylcholine, serotonin, or epinephrine. Extraction of bathing media from active testes for prostaglandin-like compounds produces a substance that stimulates inactive smooth muscle preparations and gives biochemical and biological assays for prostaglandins. A time-lag often occurs before spontaneous contractions begin in excised rabbit testes connected to a transducer. Contractions can be initiated in these preparations by adding prostaglandins.

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Higher neural control is evidently involved in the control of prostaglandin synthesis and testicular responses. Seasonal changes occur in the spontaneity of testicular contractions, as judged by tests carried out in vitro. During winter months, contractions became variable; in February and March, contractions did not develop even after an hour's incubation. Motility was consistently induced in the inactive preparations with exogenous prostaglandins. Spontaneous contractions have been observed in testes from animals as early as two weeks after parturition. All of these data indicate that prostaglandins are required for spontaneous contractions of the testicular capsule in vitro and that certain chemicals or physiological stimuli may regulate prostaglandin synthesis.

In this dual endocrine role of the testis, the same basic enzyme systems are utilized in the synthesis of both androgens and prostaglandins. Prostaglandins have been assayed for their ability to affect androgen synthesis in vitro and in vivo; they have only small effects at concentrations much larger than those required to regulate the contractions of the testicular capsule. The synthesis of androgens and prostaglandins may be dissociated into four functional units by exogenous serotonin and melatonin: androgen synthesis, prostaglandin synthesis, and lipid peroxidation resulting in hydroxylation involving chain shortening, and malonaldehyde production. The latter three systems involve lipid peroxidation where unsaturated fatty acids (dihomo- γ -linolenic, arachidonic, and 5,8,11,14,17-eicosapentaenoic acids) are converted into either malonaldehyde and hydroxylated fatty acid derivative or prostaglandins. Thus, lipid peroxidation serves three biochemical functions in the testis.

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Analyses of the physiological and biochemical effects of serotonin and melatonin reveal that they act at least partly via prostaglandins. Serotonin inhibits androgen synthesis, inhibits malonaldehyde formation, increases prostaglandin synthesis, and increases tonus and rate of testicular contractions in contracting testes. Melatonin also inhibits androgen synthesis, but has the reverse effect on the other three systems: malonaldehyde formation is increased, and both prostaglandin synthesis and testicular contractions are inhibited. The effects of serotonin and melatonin on contractions of the testicular capsule may thus be explained in part by their action on prostaglandin synthesis.

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