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THE MECHANISM(S) OF LH AND GnRH INDUCED STEROIDOGENESIS AND PLASMINOGEN ACTIVATOR IN PREOVULATORY RAT FOLLICLES

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Recent studies revealed that in addition to the cAMP-mediated action of gonadotropins on the follicle, GnRH induces steroidogenesis and ovulation, apparently by cAMP-independent mechanism(s). Here the effect of inhibitors of cyclooxygenase, indomethacin (10 μM) and of lipoxygenase, nordihydroguaiaretic acid, caffeic acid, esculetin and AA861 (100 μM) on LH- and GnRH-stimulated steroidogenesis was examined in explanted preovulatory rat follicles cultured for 6 and 24 h. Since plasminogen activator (PA) is involved in the process of follicular rupture at ovulation, it was assayed in parallel. All the inhibitors used attenuated the GnRH-induced rise in progesterone accumulation and PA activity by approx $\geq$ 50%, during the first 6 h of incubation, while they had no effect on the same when induced by LH; likewise, the inhibitors did not affect follicular estrogen accumulation in response to LH or GnRH. Nevertheless, the inhibition of progesterone accumulation and of PA activity was relieved during further 18 h of incubation and that of estrogen accumulation in the presence of GnRH was even stimulated. Further evidence of the role of the calcium in evoking follicular steroidogenesis was demonstrated by the increase in progesterone accumulation by phospholipase C (IU/ml) and diacyl glycerol (80 μg/ml), activators of the calcium and phospholipid-dependent protein kinase C. Thus, ovulatory changes may be triggered in the preovulatory rat follicles by both pathways: by LH, through cAMP mediation and by GnRH, through the mediation of Ca ions and protein kinase C. (Supported by Grant I-613-83 from the United States-Israel Binational Agricultural Research and Development Fund, BARD).

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DIETHYLSTILBOESTROL (DES) TREATMENT INCREASES PROSTATIC ANDROGEN RECEPTOR CONCENTRATION AND SENSITIVITY TO ADRENAL ANDROGENS IN RATS. M. MOGUILEWSKY, C. TOURNEMINE, J. FIET*, Centre de Recherches Roussel Uclaf, 93230 Romainville, *Hôpital St Louis, Paris, FRANCE

In order to explain the relapse observed after DES treatment of prostatic cancer patients, leading to increase doses, we have compared the effects of either a 15-day surgical castration (CX) or DES treatment, on the prostate sensitivity to adrenal androgens administration in male rats. a) DES treatment, like castration, resulted in very low plasma testosterone concentration and in largely decreased prostate weight. b) cytosolic androgen receptor concentration was much higher in the prostate of DES treated rats than in that of CX rats. c) when CX or DES treated rats (whose adrenals, unlike those of human, secrete very small quantities of androgens) were continuously administered (osmotic minipumps, s.c.) adrenal androgens in order to obtain circulating levels equivalent to those recorded in humans, the prostate weight of DES-treated rats was increased more than that of CX rats. d) when anandron (RU 23908), a pure antiandrogen, was administered concommitently to adrenal androgens, higher doses were required to completely counteract adrenal androgens activity in DES-treated rats. These results might explain the relapse after DES treatment in prostatic cancer patients. Both modes of castration result in testosterone suppression, but the unsuppressed adrenal androgens, still active after orchidectomy, might be more active after DES treatment on account of the marked increase in prostate AR.