25. ETHINYL ESTRADIOL AND HYDROCORTISONE EFFECT ON CELL PROLIFERATION AND ANGIOTENSINOGEN Fao CELLS.

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Biosynthesis of the renin substrate, angiotensinogen, is enhanced by estrogens and glucocorticoïds. The mechanism of action of ethinyl estradiol (EE_2) or hydrocortisone on angiotensinogen production and cell proliferation was studied in cultured rat hepatoma cells. Release of angiotensinogen, measured by direct RIA, from cells grown under standard conditions was greatest during the stationary phase of the growth cycle. EE_2, added to medium containing only 1% of steroid-free FCS, stimulated cell proliferation at 10^{-9} to 10^{-8}M, whereas, stimulation of angiotensinogen required 10^{-7} to 10^{-6}M. At these higher doses, cell proliferation actually slowed as angiotensinogen production increased 4-fold. Hydrocortisone at 10^{-8}M did not affect cell proliferation but decreased angiotensinogen slightly. At 10^{-7}M, cell proliferation was greatly depressed and angiotensinogen synthesis decreased to 0 within 2 months. At 10^{-5}M, cells died within 10 days and angiotensinogen production ceased after day 3. These results suggest that the effects of EE_2 on cell proliferation and angiotensinogen production occur independently. Hydrocortisone, which is necessary for maintaining the functional activity of hepatocytes, was found to be lethal to FaO cells.

3. OVARIAN FUNCTION: FOLLICLE

26. THE REGULATION OF MEIOTIC COMPETENCE BY FSH AND E_2

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The ability of isolated oocytes to resume meiosis ("meiotic competence") in culture develops between days 20-26 post partum (pp). Hypophysectomy on day 15, but not on day 22 pp, resulted in a striking decrease in the development of meiotic competence when examined on day 26 pp. This effect on hypophysectomy was completely reversed by PMSG and partially by estradiol 17β. Only FSH (NIAMD-rat FSH-B-1; 10-20 µg/dayx4), but not LH (NIAMD-oLH-21; 2-20 µg/dayx4) was able to induce meiotic competence in rats hypophysectomized on day 15 pp. When inhibitors of steroidogenesis (aminoglutethimide, 17β-formamidoandrost-4-en-3-one, or 1,4,6-androst-3-17 dione) were coadministered with FSH they inhibited its effect on the development of meiotic competence. Furthermore, when estradiol 17β was administered together with these inhibitors of steroidogenesis, the effect of FSH on the development of meiotic competence was not disturbed. These results strongly suggest that FSH, but not LH is involved in the acquisition of meiotic competence. Further, this action of FSH appears to be mediated, at least partially, by follicular estrogen production.(Supported by the United States-Israel Binational Agricultural Research and Development Fund - BARD).

27. HUMAN IN VITRO FERTILIZATION AND EMBRYO TRANSFER, PLASMA AND FOLLICULAR HORMONE LEVELS

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Twenty six patients participating in our program of in vitro fertilization and embryo transfer underwent hormonal monitoring of menstrual cycle before and after oocyte aspiration. Thirty nine oocytes were recovered and 10 embryos were transfered, one pregnancy was obtained. The content of 17 B estradiol, progesterone, prolactin, FSH and LH were determined in the aspirated follicular fluid and compared to the peripheral plasma levels.

Results: Follicular growth was closely correlated with peripheral estrogen levels. An aspiration of a preovular follicle did not lead to impaired steroid function of subsequent corpus luteum. The concentration of FSH in the follicular fluid was slightly lower than in the matched samples of plasma, but there was no difference in the LH levels. High concentration of 17 B estradiol and progesterone were determined in follicular fluid from mature follicles, both when the oocyte recovered, were fertilized and not fertilized.

Conclusions: a) Corpus luteum insufficiency is not observed following aspiration of follicle and oocyte recovery, and it is not a main cause of a non successful embryo transfer. b) Concentration of 17 B estradiol and progesterone in the follicular fluid in a preovular follicle cannot predict the success of fertilization.