37. ANDROGEN RECEPTORS: NEW APPROACH FOR OPTIMISING RECEPTOR LEVELS IN THE HUMAN PROSTATE

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Different methods for the measurement of androgen receptors in both the soluble and nuclear - pellet fractions of human prostate tissue were investigated. The benign malignant specimens were obtained either retropubically or by the trans-urethral resection (TUR) method. Our experiments suggest that the androgen binding was unaffected by the presence of proteolytic inhibitors such as phenyl-methylsulphonyl fluoride, leupeptin and aprotinin as well as by the concentration of endogenous steroids maintained in the tissue. In contrast the receptor concentration was directly proportional to the amount of sodium molybdate added to the cytosol and nuclear fractions and the assay was reliable down to protein concentrations of about 5 mg/ml. Storage at -30°C. drastically reduced the binding whilst the receptor levels of TUR chips appear to be of the same order of magnitude as those measured in the retropubic gland. Preliminary studies on the separated epithelium and stroma suggest that the receptor levels varied widely between different patients but this was accompanied by a positive correlation between stroma and epithelium.

38. A REAPPRAISAL OF DIETHYLSTILBOESTROL TREATMENT USING RAT PROSTATE.

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Since oestrogen treatment is often given to control human prostate cancer it is important that the underlying mechanisms are understood.

Intact and castrated male Wistar rats were implanted subcutaneously with about 15 mg of diethylstilboestrol (DES) in Silastic tubing and killed at various intervals. Cytosolic androgen and oestrogen receptors were measured in the prostates using the controlledpore glass bead method (Randall & Mainwaring, 1982 - parallel abstract) with [$^3$H] 5α-dihydrotestosterone and [$^3$H]oestradiol-17β as ligands. Isoenzymes were detected by incubation with the relevant substrate mixture after discontinuous electrophoresis of cytosol in 7.5% polyacrylamide gels (Mangan et. al., 1973).

Both androgen and oestrogen receptor levels dropped after castration and DES treatment reaching a minimum around 4 days, but returned to normal by 7-8 days with or without DES. Competition studies are in progress. DES had no effect on lactic dehydrogenase or acid phosphatase, but promoted the formation of several isoenzymes of glucose-6-phosphate dehydrogenase and increased the concentration of one or more isoenzymes of alkaline phosphatase and malate dehydrogenase. It appears that DES may influence gene expression in the rat prostate to alter the production of several isoenzymes. Reference: Mangan, Pegg & Mainwaring (1973) Bioch. J. 134, 129-142.

## 5. CORTICOSTEROID SECRETION etc.

39. ADRENAL RESPONSE TO ACTH IN MEN WITH RENAL FAILURE(CRF)UNDER CHRONIC HEMODIALYSIS (HD)

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In male patients affected by CRF under HD,we have reported decreased basal concentration of $\Delta_5$ adrenal androgens.If this situation is related to a decreased sinthesis of these hormones or to a blockage of specific enzymatic activities is uncknown.To evaluate this 8 male patients(26-53 yrs)in HD from 3 to 123 month on alternate days and 7 normal men (N)(25-36 yrs)have been submitted to exogenous stimulation with 1-24 ACTH(1 U i.v.) performed after a short dexamethasone suppression(2 and 1 mg,12 and 8 hrs before ACTH) and blood samples were taken until 180 min. $\Delta_5$P,DHA,DHAS,P,17OHP,$\Delta_4$A and Cortisol(F) have been evaluated by RIA (RADIM antisera,Rome,I)either directly in the plasma(DHAS and F)or after ether extraction and celite-ethylene glycole column chromatography.Results expressed as concentrations x time areas of each hormone showed in IRC a significantly (p 0.001) lower response of $\Delta_5$P(0.48±0.18 ugxmin/ml),DHA(0.66±0.27 ugxmin/ml) and DHAS (24.4±14.1 ugxmin/ml) than in N(1.1±0.22;1.0±0.27;and 27.6±13.4 ugxmin/ml respectively) On the contrary either IRC as N showed the same values for 17P(IRC:83.6±27.4; N: 106±34.2 ngxmin/ml),F(IRC:37.8±17.1; N: 49.2±9.6 ugxmin/ml) and A(IRC:0.22±0.16; N:0.21±0.51 ugxmin/ml).From these results it is possible to conclude that in men,CRF is associated wiht a decreased baseline activity and ACTH response of the $\Delta_5$steroid secreting cells while the $\Delta_4$ appears to be normals.These findings are suggestive for a specific alteration in IRC of the $\Delta_5$ steroid secretory cells which remain unexplained but appears to be typical of the desease.