

**THE USE OF TISSUE CULTURE IN THE SCREENING OF HORMONE SENSITIVITY OF ENDOMETRIAL CARCINOMA.** J. HUSTIN. University of Liège, Belgium.

Numerous clinical studies have stressed the frequent hormone responsiveness of endometrial carcinoma. Nordqvist (*Acta obstet. gynec., scand.*, 1964, **43**, 296) has demonstrated *in vitro* a direct cancerocidal effect of progesterone.

We have tried to assess the response of endometrial cancer submitted *in vitro* to various steroids. Pregnenolone (25 µg/ml of medium) markedly enhanced the survival and the cell capacity of mitosis division. Oestradiol 17-β did not influence survival. On the contrary, progesterone (60–100 µg/ml) and various synthetic progestogens induced constant necrosis without preliminary secretory conversion. This necrosis has not been encountered in non-gynaecological tumours. Progesterone must be in cell contact for several hours to display its necrotizing effect.

We suggest that endometrial cancer cells most often retain steroid binding receptors. The particular effect of pregnenolone might suggest the presence of a steroid metabolizing system affecting cell growth.

**RADIOIMMUNOASSAY OF CASEIN IN THE SERUM OF NORMAL SUBJECTS AND OF PATIENTS WITH VARIOUS MALIGNANCIES.** J. C. HENDRICK and P. FRANCHIMONT. Institute of Medicine, University of Liège, Belgium.

Radioimmunoassay of casein was carried out using the double antibody solid phase (DASP) method. Incubation was at room temperature for 24 h. This short incubation period was necessitated by the rapid degradation of labelled casein. Thus, 5 days after labelling, the casein no longer reacted with antibody but became nonspecifically bound to proteins and to DASP in the absence of specific antibody.

The characteristics of the radioimmunoassay for casein were very satisfactory, as indicated by the smallest detectable amount, the precision and the reproducibility as measured by the coefficient of variation within assay.

The immunological reaction was determined by antigenic groups specific to human

casein, there being no cross-reaction whatever with bovine casein.

Casein was not usually detectable in the serum of men or normal women who were not lactating. In contrast, all the sera of lactating women contained this natural milk product. In the patients with breast cancer before treatment, casein was found in 72%. In contrast, in benign breast lesions this phosphoprotein was found only rarely.

**PREGNENOLONE METABOLISM IN PATIENTS WITH CARCINOMA.** N. O'HIGGINS, P. CARSON and N. DESHPANDE. Hammersmith Hospital and Imperial Cancer Research Fund, London.

In patients with mammary carcinoma, low blood and urinary levels of androgens have been associated with a poor prognosis. Whether this is due to reduced adrenal synthesis of androgen or altered utilization of androgen precursor is unknown.

We have studied 20 patients with mammary carcinoma and have measured production and metabolic clearance rates of pregnenolone, which is a precursor both of the androgen, dehydroepiandrosterone (DHA), and of cortisol. The DHA:cortisol ratio did not vary between those with early and advanced disease. Of 14 patients with advanced disease treated by endocrine methods 10 responded favourably and 4 poorly. The mean DHA:cortisol ratio in the responders (1.2) was significantly higher than in the non-responders (0.5).

Pregnenolone metabolic studies may therefore provide a useful guide to predicting hormonal responsiveness in mammary carcinoma.

**SERUM OESTRADIOL 17β IN NORMAL PREMENOPAUSAL WOMEN AND IN PATIENTS WITH BENIGN AND MALIGNANT BREAST DISEASE.** L. G. SKINNER, P. C. ENGLAND, K. M. COTTRELL and R. A. SELWOOD. Clinical Research Laboratories, Christie Hospital and Department of Surgery, University Hospital of South Manchester.

Evidence exists of a relationship between ovarian function and development of breast disease. This study compares levels in premenopausal women with benign and malignant disease with the pattern of serum oestradiol 17β in normal women.

Serum oestradiol  $17\beta$  was measured throughout the menstrual cycle in 40 normal women, in 17 with fibroadenosis, in 12 with cystic disease and in 10 with cancer of the breast, by radioimmunoassay (Cameron and Jones, *Steroids*, 1972, 20, 737).

Results showed that (1) 36 of the 40 normal premenopausal women exhibited a constant pattern, but concentrations varied with age; (2) oestradiol was low during the follicular phase of the normal cycle ( $35.3 \pm 4.4$  pg/ml), rose to sharp pre-ovulation peak ( $192.9 \pm 12.7$  pg/ml) and plateaued during the luteal phase ( $67.3 \pm 1.5$  pg/ml); (3) patients with fibroadenosis showed a concentration pattern not significantly different from normal; (4) in patients with cystic disease, concentrations were significantly higher during the luteal phase; (5) patients with breast cancer considered as a group showed no consistent divergence from normal pattern.

**OESTROGEN AND ANDROGEN RECEPTORS IN HUMAN BREAST CANCER.** E. ENGELSMAN, C. B. KORSTEN, J. P. PERSIJN and F. J. CLETON. Netherlands Cancer Institute, Amsterdam.

Oestrogen and androgen receptors were determined in human breast cancer tissue samples.

Oestrogen receptors were found in 41% of 157 primary cancers and in 46% of 84 metastatic cancers. Androgen receptors were present in 18% of 43 primary tumours and in 22% of 36 secondary lesions.

A strong correlation was found between the presence of oestrogen receptors in metastatic tumour tissue and the response to endocrine therapy: 31 objective remissions in 39 receptor positive cases and only 4 objective remissions in 45 receptor negative cases. For androgen receptors no such correlation was detected in a small number of evaluable patients.

In 12 patients the presence or absence of oestrogen receptors did not correlate with the objective response to endocrine therapy. Some cases had to be recorded as a failure, when clinical improvement was present but without measurable tumour regression. The receptor content need not be the same in different metastatic deposits in one patient; this might explain some discrepancies.

**OESTROGEN RECEPTORS IN HUMAN BREAST CANCER.** G. LECLERCQ, J. C. HEUSON and W. H. MATHIELEM. Institut Jules Bordet, Brussels, Belgium.

Tumour tissue samples from 166 primary and 136 metastatic breast cancers were analysed for oestrogen receptors. Cytosol fractions were incubated with increasing amounts of  $^3\text{H}$ -oestradiol- $17\beta$  (LeClercq *et al.* *Eur. J. Cancer*, 1973, 9, 665). Unbound radioactivity was removed by charcoal-dextran. Receptors were detected in 72% of the primary and 54% of the metastatic tumours. In 86% of the "positive" cytosols, the dissociation constant of the binding reaction varied between 0.5 and  $20 \times 10^{-10}\text{M}$ ; in the remaining 14% the range was from 20.1 to  $132 \times 10^{-10}\text{M}$ . At the time of mastectomy primary tumours were examined together with the corresponding invaded axillary lymph nodes. A statistically significant correlation was observed between the amounts of receptors at both sites. In tumours the concentration of binding sites varied from zero to 1480 femtomol/mg protein. The distribution of the cytosols in regard to this parameter was continuous and inversely related to it. It is suggested that the "positive" and "negative" cytosols may not be qualitatively different, the latter simply containing receptors in amounts undetectable by the current methods. Receptors were never found in various oestrogen non-target tissues or in sera.

**PREDICTION OF RESPONSE OF DISSEMINATED BREAST CANCER TO ADRENALECTOMY AND OOPHORECTOMY USING COMPUTER AIDED EVALUATION OF CLINICAL PRESENTATION.** D. J. LEAPER and J. C. HORROCKS. Leeds General Infirmary.

Difficulties in predicting response to hormonal ablation are well known; criteria employed to make such a distinction vary from "clinical impression" through discriminant function to more recently reported assessments (*e.g.* oestrogen receptors). These methods however are to some degree fallible, time-consuming and difficult to perform.

An attempt to predict response to endocrine ablation in 100 patients using a computer aided analysis of some 18 clinical signs and symptoms has been made. Using a