

3. Steroid receptors help select treatment for breast cancer patients, W.L. MCGUIRE, The University of Texas Health Science Center, San Antonio, Texas

Recently, it has been shown that those axillary node positive patients whose breast tumors lack the ability to bind estrogen (do not have estrogen receptor) have the most rapidly growing tumors and have a very high probability of returning with metastatic disease. Since the response rate of estrogen receptor negative patients to cytotoxic therapy is appreciable, they should be treated with combination chemotherapy. Those patients who have positive axillary nodes and estrogen receptor in their tumors have a somewhat more favorable prognosis since the tumor behaves less aggressively. Since their tumor contain estrogen receptor, they are ideal candidates for adjuvant endocrine therapy, especially one of the new antiestrogen compounds. The routine measurement of estrogen and progesterone receptors provides a rational basis for treatment decisions in advanced breast cancer. Patients whose tumors lack both receptors rarely respond to endocrine therapy and are ideal candidates for combination chemotherapy regimens. Patients with tumors containing estrogen receptor but not progesterone receptor have a low response rate to endocrine therapy (25%) and deserve trials of both endocrine and cytotoxic therapy either in sequence or combination. In those patients with both estrogen and progesterone receptors, the response rate to endocrine therapy is very high (30%) and a good response to endocrine therapy is to be expected.

4. Occupied and unoccupied oestradiol receptors in nuclei and cytosol from human breast tumours, T. THORSEN, Hormone Laboratory, University of Bergen School of Medicine, Bergen, Norway

A solid phase hydroxylapatite (HAP) exchange assay has been used to estimate occupied and unoccupied oestradiol receptors in nuclei and cytosol from 85 human breast tumours. Results have been related to the content of progesterone receptor in the cytosol. Incidence of occupied nuclear receptor was high (91%) in tumours containing both oestradiol and progesterone cytosol receptors and low (47%) in tumours containing oestradiol receptor only. In 13 out of 49 tumours with cytosol oestradiol receptor (21%) no nuclear receptor could be detected. Ten of these were progesterone receptor negative. The results indicate that translocation defects may be present in human breast tumours. In eight tumours that were oestradiol receptor negative and progesterone positive by a conventional dextran-charcoal assay, occupied oestradiol receptor could be detected in the cytosol, and in 6 cases nuclear receptor was present. Seven of these patients were below 50 years of age.

It is concluded that the measurement of occupied or total oestradiol receptor in cytosol and nuclei may be a valuable supplement to existing methods for the determina-

tion of hormone dependency in breast tumours.

5. Relationship of estradiol receptors to tissue and serum alpha-lactalbumin and serum prolactin in human breast cancer, A. MOLTENI, R. BAHU, E. FORS, M. MANG-KORNKANOK and D. ALBERTSON, Dept. of Pathology, Northwestern Univ. Med. Ctr., Chicago, Ill. 60611

Estradiol (E2) binding activity was studied in 509 primary mammary tumors by the sucrose density gradient method and 38% of them were positive. The highest percent of positive binding (67%) was found in infiltrating lobular carcinoma (CA) and the lowest (17%) in the comedo type of infiltrating ductal Ca. This method correlated well for positive or negative binding activity with immuno-fluorescent techniques. Determinations of E2 receptors in metastatic lymphnodes of breast tumors showed a higher incidence of positive binding (70%) likely due to increased numbers of malignant cells with less necrosis and fibrosis. An indirect immunofluorescence technique was also used in the same neoplasms to detect alpha-lactalbumin ( $\alpha$ -LA) and 44% of them were positive. Infiltrating ductal CA had the highest incidence of positive  $\alpha$ -LA (63%) while lobular CA had the lowest (7%). Presence or absence of E2 binding activity and  $\alpha$ -LA did not correlate. Moreover there was no correlation between high concentrations of tumor E2 receptors and serum concentrations of  $\alpha$ -LA and prolactin in the same patients. E2 binding activity was not specific for breast tissues as it was also found in neoplasms of other organs (kidney, thyroid, pancreas) while  $\alpha$ -LA was detected only in normal or neoplastic breasts. These results suggested that breast cells with E2 binding activity and those secreting  $\alpha$ -LA are likely to be different even when they are histologically indistinguishable.

6. Diagnostic and prognostic methods, E. ENGELSMAN, Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, The Netherlands (see Addendum)

7. Receptor studies and survival in human breast cancer, G. CONCOLINO, A. MAROCCHI, C. D'ATTOMA, G. RICCI, L. CARDILLO<sup>1</sup> and L. PICARDI<sup>2</sup>, Istituto di Clinica Medica Generale et Terapia Medica V, Università di Roma; <sup>2</sup>Istituto di Clinica Chirurgica Generale e Terapia Chirurgica I, Università di Roma; <sup>1</sup>Ospedale Regina Apostolorum Albano Laziale, Roma

A comparison has been made between the survival rates in two groups of mastectomized breast cancer patients. All were given radiotherapy, but in one group (22 patients) receptor studies were performed whilst in the other (24 cases) they were not performed.

Oestradiol, progesterone and dihydrotestosterone cytosol receptors were studied by means of agar gel electrophoresis at low temperature or protein sulphate precipitation in

22 cases of human breast cancer. Of 17 patients in whom the tumour was receptor positive, 11 received endocrine treatment (ovariectomy alone, or ovariectomy associated with tamoxifen in 7 premenopausal women, and tamoxifen only in 4 postmenopausal women). Two patients with a receptor positive and 1 with a receptor negative tumour, all of whom received endocrine treatment, died from carcinomatous disease 1-3 years after radical mastectomy, and one with a receptor positive tumour died from senility. 13 patients (11 with a receptor positive and 2 with a receptor negative tumour) are still alive 2-5 years and 5 almost 1 year, after mastectomy. Thus only 2 out of 17 patients with receptor positive cancer and one out of the 3 patients with receptor negative cancer died 1-3 years after mastectomy.

The retrospective study of 24 women with breast cancer who were treated by radical mastectomy, and also ovariectomy in five women presenting with lymphnode metastases or of child bearing age, revealed that 4 patients, of whom 1 was ovariectomized, died from carcinomatous disease 2-3 years, and one (ovariectomized) from cardiovascular accident 2 years after radical mastectomy. Seven of the remaining 19 patients (1 ovariectomized) are still alive after more than 6 years, 10 (2 ovariectomized) after more than 2 years and 2 almost one year after surgery.

From a comparison of the two groups it becomes clear that the high survival rate in the latter group of patients is presumably due to the presence of a hormone dependent tumour. Whilst receptor studies may be employed in determining the choice of treatment their main usefulness is to be found in evaluating the prognosis.

8. Endocrine treatment of breast cancer, O. PEARSON, Case Western Reserve, Cleveland, Ohio, U.S.A.
9. Suppression of corpus luteum function by D-Leu<sup>6</sup>(des-Gly-NH<sub>2</sub><sup>10</sup>, Proethylamide<sup>3</sup>) GnRH in premenopausal women with breast cancer, G. TOLIS, A. CHAPDELAIN, K. ROBERTS, N. PAPANDREOU, M. PAPACHARALAMBOUS and N. FRIEDMAN, Royal Victoria Hospital, Maisonneuve Hospital, Aghios Panteleimon Hospital and Abbott Labs, Montreal, Athens, Chicago

Mastectomy, radiotherapy, adjuvant chemotherapy and ovariectomy are employed in conjunction for the treatment of premenopausal breast cancer. In an effort to suppress ovarian function we administered an analogue of GnRH, which in the experimental animal induces down regulation, to three such patients. 10 µg were injected daily for 8 days beginning on the 7th, 8th or 9th day of the cycle. Serum FSH, LH, estradiol, progesterone and prolactin (PRL) were measured daily prior to injection. In addition on days 1, 2, 5 and 8 blood was collected continuously for 12 h to assess pituitary FSH and LH secretory release patterns. The acute increments in LH and FSH were 8- to 16-fold and 5- to 9-fold, respec-

tively, during the first day; the increments however during days 5 and 8 were decreased by 50 %. No change in basal FSH, LH and PRL levels was recorded throughout the sampling period of 8 days; the values of LH and FSH remained within the range for the follicular phase. Plasma estradiol in 2 out of 3 increased to midcycle levels by the 5th post-injection day but was not followed by a mid-cycle LH surge nor by a rise in serum progesterone which remained at follicular levels. In all three patients vaginal bleeding occurred 4-6 days earlier than expected thus shorting the luteal phase in one cycle and causing anovulation in two cycles. Normal length cycles were recorded in the subsequent months.

The above data indicate that repetitive administration of this GnRH analogue can effectively suppress corpus luteum formation and/or function in premenopausal women with breast cancer and may thus be used in the future as an adjuvant for the treatment of this disease or as an ovulation inhibitor. The reestablishment of regular cycles upon discontinuation of this peptide indicates the reversibility of the above effect on ovulation and underscores the potential of this agent as a contraceptive.

#### PROSTATE CANCER

10. Carcinoma of the prostate: endocrine aspects of aetiology, G.D. CHISHOLM and F.K. HABIB, Department of Surgery/Urology The Medical School, Edinburgh EH8 9AG, Scotland

The evidence for an endocrine (androgen/oestrogen) role in the aetiology of carcinoma of the prostate will be examined from 3 groups of data.

1. Epidemiological data: Necropsy studies have shown that patients with cirrhosis of the liver have less prostatic cancer than controls. Anthropometric studies have shown no characteristic differences from controls but patients with cancer of the prostate tend to have more body hair and to be less obese. The differences in the incidence between negroes in Africa and USA have been ascribed to genetic differences. Sexual activity, marital status, circumcision and the number of children have been studied in respect of the incidence of carcinoma of the prostate and the findings will be reviewed. The data concerning the relationship between benign prostatic hypertrophy and prostatic cancer will be examined.

2. Plasma measurements: Sex hormone changes with age have shown that there is a decrease in testosterone, dihydrotestosterone (DHT), androsterone and dehydroepiandrosterone; there is a marked increase in oestradiol and SHBG, LH and FSH also increase with age.

In attempting to define sex hormone differences between normal controls, benign prostatic hypertrophy and carcinoma of the prostate, differing results have been reported but most series have shown no differences for