

profiles on treatment with the patient's own control cycles showed that nine were resistant to HMG, eleven had an accelerated follicular growth and the remaining seven showed an immediate excessive increase in oestradiol which was not followed by ovulation. Examination of the luteal phases (progesterone levels) demonstrated that on treatment ten were improved whilst the remaining seventeen were either unaffected or were worse. Five

patients became pregnant during HMG treatment. It was impossible to predict from control hormonal profiles how a patient would respond to HMG.

#### Reference

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### POSTERS

#### BREAST CANCER

39. Significance of plasma sex hormone binding globulin (SHBG) binding capacity in breast cancer and fibrocystic breast disease, G.P. GAIDANO, L. BERTA, E. ROVERO, P. ANSELMO, P. ROSATTI and C. NAVELLO, Istituto di Medicina Interna dell'Università di Torino, II Cattedra di Patologia Speciale Medica, Strada S. Vito 34, 10133 Torino

Plasma sex hormone binding globulin (SHBG) binding capacity was determined in women with breast cancer and with benign breast disease in order to compare these clinical conditions with respect to age of onset of disease and to plasma hormonal characteristics.

14 women with breast cancer were subdivided into 2 groups: 6 premenopausal women aged 28 to 45 years in the oestrogenic phase of the menstrual cycle and 8 postmenopausal women aged 50 to 75 years. The patients never received any treatment (hormonal or cytostatic) and did not show hepatic or renal failure. Neoplasia had been recognized and surgically removed 3 months to 2 years prior to the study. In 9 women aged 18 to 35 years the diagnosis of fibrocystic breast disease was made by biopsy. The control groups consisted of 19 premenopausal women aged 20 to 45 years in the oestrogenic phase of the menstrual cycle and 8 postmenopausal women aged 50 to 75 years.

With respect to the controls, mean values of plasma SHBG binding capacity (expressed as  $\mu\text{g}$  of DHT bound/100 ml plasma) were significantly lower in premenopausal women with breast cancer ( $1.68 \pm 0.6$ ,  $P < 0.01$ ), while no difference was observed in the other groups. Plasma prolactin and  $17\beta$ -oestradiol did not show any difference in all the groups examined as compared to controls. Mean values of SHBG binding capacity observed in women with fibrocystic breast disease were significantly higher than those of premenopausal breast cancer patients ( $P < 0.02$ ).

Our data support the hypothesis that breast cancer in pre- and postmenopausal women are aetiologically two distinct diseases.

The lower levels of SHBG binding capacity observed in premenopausal women may be related to increased adrenal secretion of androgens which have been shown to decrease SHBG synthesis. On the other hand, a primary de-

crease of SHBG cannot be excluded. In this condition, the oestrogen "free fraction" rises and could play a role in the evolution of neoplasia.

In fibrocystic breast disease different plasma hormonal characteristics have been suggested: increase of adrenal androgen levels; relative or absolute progesterone deficiency. The balance of all these factors as well as plasma total oestrogen levels in the normal range, could explain the behaviour of the SHBG binding capacity observed in our cases.

Assay of plasma SHBG binding capacity could play a significant role both in epidemiological studies of populations at risk for different types of breast cancer and in monitoring the evolution of fibrocystic breast disease.

40. Neutral urinary steroids and estrogen receptors in breast cancer, D. VANDEKERCKHOVE, E. VANLUCHENE, W. AERTSENS and J. DE BOEVER, Dept. Gynaecology, Academic Hospital, Ghent

We determined urinary 11-deoxy-17-ketosteroid (11-DOCS) and corticosteroid excretion in 49 early breast cancer (EBC) patients and in 25 control patients with no evidence of cancer or endocrinological disease. In both groups of hospitalized patients, two consecutive 24-h urine specimens were collected, both before mastectomy and before the various other surgical operations. In 34 EBC-patients a collection was also obtained on the 10th postoperative day. Urine samples were analysed by capillary gas chromatography (1). In 35 EBC-patients the estrogen receptor (ER) content of the tumor was determined: 13 patients had no detectable ER-levels while in 22 patients 250 to 19,541 fmol ER per gram tissue were measured.

No significant difference in pre-operative 11-DOCS excretion between controls and EBC-patients was found. In the post-mastectomy specimens 11-DOCS levels were significantly lower ( $P < 0.1$ ) than in the pre-operative samples, but were not different from the control group. These findings are at variance with the observation that a majority of EBC-patients had subnormal 11-DOCS-excretion (2), but show a lowered post-operative excretion. We found no significant difference between 11-DOCS excretion in controls, ER-negative

and ER-positive patients. This observation does not confirm previously reported results (3). However, we observed a significant negative correlation between both the androsterone-aetiocholanolone (A/Ae) ratio ( $r = -0.60$ ,  $P < 0.01$ ) and the allo-tetrahydrocortisol-tetrahydrocortisol (aTHF/THF) ratio ( $r = -0.56$ ,  $P < 0.01$ ), and the logarithm of the ER-concentration. This correlation was especially good for the 5 $\alpha$ -reductase products androsterone ( $r = -0.36$ ,  $P < 0.1$ ) and allo-tetrahydrocortisol ( $r = -0.61$ ,  $P < 0.005$ ). Contrarywise no significant correlation was found between the ER-concentration and the 5 $\beta$ -reduced metabolites. On the other hand there was no significant difference in A and 5 $\alpha$ -THF values between ER-negative and ER-positive patients. These observations suggest an inverse relationship of 5 $\alpha$ -reductase activity with the ER-concentration in breast cancer.

#### References

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41. Estradiol receptor activity (ER) in right or left sided breast cancer, L. BEEH, A. KOENDERS, G. PIETERS, A. SMALS, J. HENDRIKX, Th. BENRAAD, P. KLOPPENBORG, Departments of Medicine and Radiology, University of Nijmegen, Nijmegen, The Netherlands
42. Estrogen receptors in normal and malignant human breast tissues, J. DE BOEVER, K. DE GEEST, G. VAN MAELE<sup>1</sup> and D. VANDEKERCKHOVE, Department of Obstetrics and Gynecology and <sup>1</sup>Medical Information Centre, Academic Hospital, University of Ghent, B-9000 Ghent, Belgium
- Cytoplasmic estrogen receptors (ER) were measured in extracts of normal breast tissue and of the mammary tumour specimens of 180 breast cancer patients - 142 patients with early breast cancer and 33 with advanced breast cancer. Receptors were measured with a Dextran-coated charcoal technique employing <sup>3</sup>H-estradiol and diethylstilbestrol. Steroid receptor (ER) binding parameters were calculated from Scatchard plots. 58% of all breast cancer tissues were estrogen receptor positive (ER+) with binding capacities of 3.1 to 2545 fmol of ER/mg protein and with dissociation constants (Kd) between 0.1 and  $7 \times 10^{-10}$  mol/l. 41% of the breast cancer tissues did not contain measurable quantities of ER and were considered to be negative (ER-). 42 normal breast tissue samples were examined for ER content and all were found to be negative (ER-). Both ways of expressing the ER content of tissues: fmol/mg protein of fmol/g wet tissue were found to be equally suitable and reliable (correlation  $r = 0.99$ ;  $P < 0.001$ ). Two more good correlations were found: between Kd and the binding index (BI) and between ER levels and BI.
- In the early breast cancer group ER+ tumours were found in 65% of the postmenopausal patients and in 50% of the premenopausal patients. Postmenopausal patients had significantly higher ( $P < 0.01$ ) ER levels.
- Multivariate analysis revealed no significant differences between ER+ and ER- primary tumours of pre- and postmenopausal patients in relation to known prognostic factors: histology, tumour volume, tumour location in the breast, clinical stage and axillary nodal status. In addition there was no correlation between these factors and ER levels.
- In the group with advanced breast cancer 64% of the tumours were ER+ for both pre- and postmenopausal categories.
43. Immunofluorescent observation of prolactin receptors in cultured mammary carcinoma cells, H. TAKIKAWA<sup>1</sup>, R. HORIUCHI<sup>1</sup>, S. TANAKA<sup>1</sup> and K. TARUSAWA<sup>2</sup>, <sup>1</sup>Institute of Endocrinology, Gunma University, Maebashi, and <sup>2</sup>Japan Immunoresearch Laboratories, Takasaki, Japan
- The presence of prolactin receptors in mammary carcinoma has been reported by a number of investigators. It is accepted that prolactin plays an important role in carcinogenesis of mammary tumours. Data will be presented on the immunofluorescent observation of the receptor in DMBA induced rat mammary carcinoma. Tumours were induced in female Sprague-Dawley rats with a single dose of DMBA in cotton seed oil given orally. Tumours were rapidly excised and after removal of necrotic parts cut into small pieces. The tissue pieces were incubated with collagenase dissolved in Dulbecco's modified Eagle's medium supplemented with foetal calf serum. After filtration, the cell suspension was centrifuged and the cell pellet suspended in the medium,