

**316** Anti-tumor effect of Gn-RH against DMBA-induced rat ovarian cancer. T.Maruuchi, T.Oda, M.Nakanami, S.Motomura, T.Nishida, Dept.Obst.and Gynec., Natl.Kokura Hosp., Fukuoka.

Anti-tumor effect of GnRH was evaluated using S.C. xenografts of DMBA-induced rat ovarian cancer. A dose of 1-2 $\mu$ g of GnRH was given daily for 8 weeks into peripheral areas of S.C. xenografts. Anti-tumor effect was determined from change of tumor size, histological evaluation. Also determined were serum LH, FSH, estrogen and progesterone of tumor bearing rats. GnRH-treated group showed markedly decreased serum levels of LH, FSH, and progesterone. No significant difference was observed between GnRH-treated group and control group in the evaluation of tumor size. However, histological evaluation showed prominent central necrosis and proliferation of connective tissue of S.C. tumors in GnRH-treated group. In conclusion, it was suggested that GnRH may yield favorable anti-tumor effects with down regulation of serum LH and FSH levels.

**317** Enhancement of anti-neoplastic effects of CDDP by inhibitors by PKC activity. Y.Kikuchi, J.Hirata, H.Sasa, T.Kita, T.Tode\*, I.Nagata, Dept.Obst and Gynec., Natl.Def.Med.Coll., Saitama, \*Dept.Obst and Gynec., Shimizu Kousei Hospital, Shizuoka.

Two human ovarian cancer cell lines derived from serous cystadenocarcinoma and clear cell carcinoma of the ovary were established and designated MH and KK, respectively. Both KK and MH cells have produced CA125 in the culture medium. IC<sub>50</sub> of KF, KK, MCF-7 and MH cells were 0.41 $\mu$ M, 0.95 $\mu$ M, 2.10 $\mu$ M and 3.28 $\mu$ M, respectively. Degree of resistance to CDDP of KK and MH cells was about 2-fold and 8-fold higher, compared to that of KF cells. As the degree of resistance to CDDP increases, PKC activity in the resistant cells was higher. In addition, to elucidate relevance of PKC activity in the cancer cells to the degree of resistance, we examined changes of sensitivity of each cell line to CDDP in the presence of TPA or when preincubated with TPA for 1 h. Although KF cells showed resistancy to CDDP in the presence of 10nM or 100nM TPA, the KF cells became more sensitive to CDDP in the presence of 1 $\mu$ M TPA, while 1 h preincubation with TPA did not give any effect with regard to sensitivity to CDDP. Sensitivity of the KK cells to CDDP was reduced in the presence of 10nM TPA. Interestingly, sensitivity of the KK cells to CDDP was lost by 1 h preincubation with 1 $\mu$ M TPA.

**318** Basic and clinical studies on combined administration of Cisplatin and Etoposide in treating ovarian cancer. N.Usui, Y.Furugen, G.Mah, R.Miyazaki, M.Suzuki, M.Takada, Dept. Obst.and Gynec., Juntendo Univ. Sch. Med., Tokyo.

As second line chemotherapy in treating ovarian cancer, we studied the usefulness of combined intraperitoneal administration of EP (Etoposide, Cisplatin). In experiments in which Etoposide (3  $\mu$ g/ml) and CDDP (0.4  $\mu$ g/ml) were added separately and simultaneously to cultured HUAO and RMUG cells, the simultaneous addition group displayed higher growth inhibition rates against the respective cell strains of 74.4% and 66.4%. At the time of EipPip (intraperitoneal administration of E 200mg and intraperitoneal administration of P 100mg) the area under the curve of intraperitoneal fluid/serum was 2.99 for Etoposide, which showed a lower value than CDDP. The clinical responses of EipPip was CR in 1 case and NC in 4 cases, for EivPip they were NC in 1 case and PD in 1 case. Side effects were slighter in EipPip than in EivPip, and no case was noted requiring treatment for chemical peritonitis.

The EipPip treatment method is safe, and hereafter its usefulness as second line chemotherapy is anticipated.