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EVIDENCE OF EGF LIKE FACTORS IN OVARIAN CARCINOMAS
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Cellular proliferation is potentially stimulated by a family of hormonally active polypeptides, the growth factors. Growth factors have the potential to induce cellular transformation if they act at the wrong time or in the wrong place. Factors inducing cell transformation have been shown to be a relative to epidermal growth factor (EGF) and interact with cellular receptors for EGF (EGF like factors). The aim of this study was to investigate ovarian carcinomas for the presence of EGF like factors (EGF-F) in correlation to clinical parameters. Specimens of ovarian carcinomas and nonmalignant tissues were extracted with 1 M acetic acid, centrifuged and the supernatants analyzed for the presence of EGF-F by a EGF radio receptorassay. The factor content is expressed as EGF competing activity in ng EGF units/mg protein. In extracts of nonmalignant tissues, i.e. normal ovaries and myometrium, and ovarian carcinomas EGF-F could be detected. However, the factor contents of the different extracts varied widely. In nonmalignant tissues factor levels did not exceed 6 ng EGF units/mg. 18/42 ovarian carcinomas contained high factor concentration between 6-17 EGF units/mg. Patients were separated in two groups with low (<6 ng) and high (>6 ng) EGF-F tissue levels. Both groups were correlated with clinical data. No differences were noticed to histological subtype and steroidhormonereceptorstatus. Low residual tumorrest (< 2 cm) after primary surgery was found in 11/20 cases with low factor content compared to 4/15 cases with high factor content. The responderate to a cis-platinum combination chemotherapy in the group with low factor concentration was: 4/21 progressive disease (PD) 3/21 no change (n.c.) and 14/21 remission (CR+PR). The results in the group with high factor concentration were: 9/24 PD, 5/14 n.c. and 0/14 CR+PR. Differences in the survival time of both groups were also noticed. However, the case number is too low for detailed statistical analysis. These results let assume that the biological behaviour of ovarian carcinomas could be influenced by its content of EGF like growth factors.

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CA 12-5 SERUM LEVELS AND HISTOLOGICAL FINDINGS AT SECOND LOOK IN PATIENTS WITH OVARIAN CANCER
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CA 12-5 is a well established tumor marker in ovarian cancer, especially for serous cystadenocarcinoma. There is no doubt about the fact, that the oncofetal antigen, determined with a radioimmunoassay by the means of a monoclonal antibody demonstrates a high sensitivity but is less reliable concerning specificity. From January 1984 until October 1985 we measured CA 12-5 serum levels in 130 patients with histologically proven ovarian cancer.

1. In 130 patients with ovarian cancer 98 cases presented elevated CA 12-5 levels.
 2. When CA 12-5 was elevated at the time of primary surgery (n=30), after 6 cycles of CAP second look revealed 21 patients with residual tumor, only 14 of those with predicting persistence of CA 12-5; thus showing 7 patients with residual tumor and negative serum values.
 3. On the other hand positive serum values of CA 12-5 at the time of second look always correlate with persistent tumor.
 4. In patients with clinical evidence of progression CA 12-5 was positive in all cases.
- We like to draw the following conclusions. CA 12-5 is unable to precisely predict residual tumor in patients undergoing second look, so that negative serum values may be falsely negative. On the other hand positive values indicate that tumor persistence can be expected.

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CA 125 IN TUMOR TISSUES, CYST FLUIDS, CERVICAL MUCUS AND SERUM. H.W.A. de Bruijn, M.S. Schilthuis, M.J. Duk, J.Bouma, G.J. Fleuren, and J.G. Aalders.

CA 125 is a high molecular weight glycoprotein, first discovered in ovarian cancer. In healthy women, we found extremely high levels of CA 125 in cervical mucus (median 65,500 U/ml, n=23) and in the serous fluid from the cavity uteri (median 27,900 U/ml, n=8), but normal levels were found in the blood serum samples (<35 U/ml). Immunohistochemistry demonstrated the presence of CA 125 in the tall columnar cells of the endocervix, and also in normal endometrium. We conclude that CA 125 is a normal secretory product of the female genital tract. Although not tumor-specific, serum CA 125 estimations were very useful in monitoring the effect of therapy in patients with ovarian and endometrial cancer.

Immunohistochemistry demonstrated that CA 125 was present in 80% of the malignant nonmucinous epithelial ovarian cancers and in benign cystadenomas. In cyst fluids from ovarian tumors, CA 125 levels ranged from 22,000 U/ml to 2,140,000 U/ml in both benign and malignant ovarian tumors while levels from 1,000 to 17,000 U/ml were found in mucinous tumors. Serum levels were not related to cyst fluid CA 125, but were dependant on the presence or absence of infiltrative growth of the primary tumor. Pre-operative serum CA 125 levels were elevated in 96% of the patients with ovarian cancer, but normal in most patients with benign ovarian tumors. Progressive disease was associated with rising levels in 72 of 75 patients. In endometrial cancer, 27 of the 110 patients showed raised levels of serum CA 125. The presence of CA 125 was demonstrated in all frozen sections of endometrial cancer tissue (12 patients). Raised serum values were associated with extra-uterine tumor growth and vessel invasion of tumor cells. Increasing serum levels of CA 125 preceded the clinical discovery of relapse in patients with ovarian cancer (in 15/19) and with endometrial cancer (in 5/12). Dep. Of Obstetrics and Gynaecology, University Hospital, Oostersingel 59, NL-9713 EZ Groningen, the Netherlands.

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EXPERIENCES WITH THE HUMAN TUMOR STEM CELL ASSAY (HTSCA) & ITS MODIFICATIONS FOR CULTURING GYNAECOLOGICAL TUMORS
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Chemosensitivity of malignant tumors can be estimated using the HTSCA. Working with the test since 1982 we found the assay to be useful to predict chemosensitivity of ovarian- and breast-carcinomas (Tab.1). Among the difficulties we had bad cloning efficiency (c.e.) and cell clumping should be mentioned. When working with small quantities of biopsy material we sometimes were unable to obtain a sufficient number of cells to perform the test. To avoid the problems mentioned above we modified the colony assay by using a continuous drug exposure and a capillary technique. Results (Tab.2) if cells and drugs were incubated continuously more colonies per seeded cells could be noticed compared to the 1h drug exposure; moreover the tendency to form clumps was found to be lowered. Comparing the Petri dish method with the capillary technique the c.e. was found to be significantly increased. In the Petri dish culture system 0.5×10^6 cells seeded produced a mean of 30 colonies, in the capillary technique 9.3×10^3 cells produced a mean of 58 colonies.

Tab.1 tumor	no. of patients	S/S	S/R	R/S	R/R
ovarian	24	13	3	1	7
breast	12	6	2	-	4

S/S: sensitive both in vitro and in vivo; S/R: sensitive in vitro, resistant in vivo; R/S: resistant in vitro sensitive in vivo; R/R: resistant both in vitro & in vivo

Tab.2 Colony growth (a) and cell clumping (b) of 1-h and continuous drug exposure in the HTSCA

a) median number of colonies/ 0.5×10^6 cells	
tumor	1-h drug exposure
breast (n:32)	26
ovarian (n:46)	30
b) median number of aggregates/ 0.5×10^6 cells	
tumor	1-h drug exposure
breast (n:32)	13
ovarian (n:46)	11

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