Chemotherapy in the treatment of ovarian cancer.

(The Cancer-Chemotherapy-Sensitivity-Test)

Prof. Dr. Hans Limburg
Direktor der Universitäts-Frauenklinik Homburg-Saar

The varying reactions of human tumours of the female genitalia especially of ovarian cancers to modern cytostatic drugs were examined with the aid of primary tissue cultures in vitro.

The cultivations are performed in the Leighton tube by means of the trypsinizing metheod in accordance with DULBECCO and VOGT. The total material evaluated to date includes more than 1400 explanted human tissues the success rate being 80 %; in ovarian cancers 94%.

The primary cultures include normal squamous epithelium of the cervix, carcinoma in situ, cancer of the cervix and corpus, ovarian cancer and ovarian carcinoma ascites. With the aid of these tissue cultures examinations were carried out to observe the varying reactions of tumour cells to cytostatic drugs, such as : Endoxan, Mitomen, Methotrexate, Methylhydrazin, SPI 77, Thio Thepa, Trenimon and Vinblastine. Adapting the dosage of the chemotherapeutic substances in vitro to the actual conditions of the clinical treatment it has been possible in 300 cases to judge the probable efficacy of the substance. This "Cancer chemotherapy sensitivity test" shows completely different individual reactions from the completely resistant culture to the cytolytic destruction of the cell monolayer, although the tumour morphology may be equal or similar. By the test, one is in a condition to apply an individually determined cytostatic therapy to every kind of tumour provided that at least one of the drugs is effective. The clinical results of selective chemotherapy of cancer of the female genitalia are demonstrated by the survival rates and clinical criteria of those treated as compared to those without selective chemotherapy.

An accurate objective response index based on gross tumour regression is possible in patients previously receiving the TNM-classification before definitive treatment. The classification which is based as a rule on simple clinical examination is inappropriate. According TP, which takes into account the findings at operation should be used following the recommendations of the International Union Against Cancer (UICC), Geneva 1966.

In the patients under investigation the implantation of tumour masses or metastases were present within the peritoneal cavity including the omentum, small intestine, mesentery, liver or other viscera (M 1 b) and in several cases outside the peritoneal cavity (M 1 c).

Any major effect of chemotherapy on survival should be discernible, unless the histological classification of the epithelial tumours of the ovary is provided after the proposal of the Cancer Committee of the International Federation of Gynecology and Obstetrics, August 1961. A longer survival of Stage IV patients could reflect an

originally slower growing neoplasm, a low potential malignancy of a highly differentiated type in the histological specimen.

Therefore, serous and mucinous cysts of ovarian cancer as well as endometroid malignant tumous of the ovary have been eliminated from the patients under study. The remaining collective consists of undifferentiated carcinoma of the ovaries. The homogeny of the clinical stage of the disease and of the growth characteristics of the tumour provides a comparative appraisal of chemotherapy for ovarian cancer.

The Table I demonstrates the medium survival rate in days of a selective chemotherapy after the sensitivity test was performed in 25 patients contrasted with 14 without chemotherapy and 15 with conventional chemotherapy without the sensitivity test. The preponderance of advanced disease in this series was evident since there were 10 cases with tumour masses outside the peritoneal cavity, compared to 2 cases without test and 4 cases treated with no cancerostatic agent.

The data shown reveal a rise of mean survival time by application of cytostatic drugs from 82 to 283 days corresponding to 71%. The average duration of life span was risen from 283 to 527 days in the course of selective chemotherapy after the sensitivity test was employed. 7 out of 25 patients treated achieved excellent remissions consisted of total regression of all palpable masses, pleural effusions, and ascites associated with a return to a normal living routine.

The t-test (student distribution) of survival rates revealed a statistical significance of p smaller than 0.01 and 0.001, respectively.

The Table II correlates the survival time in the three therapeutical different groups between patients died and survivors expecting further prolongation of their life span. Thus the one year survival is 33% without and 64% after sensitivity testing. The two year survival still approximates in both groups at 20% but still gain significant difference with the prolongation of the observation time. After three years only 12% are alive in the tested group with selective chemotherapy.

In conclusion one may say the extremely low percentage of one year survivors in Stage IV cases as confirmed in other series with palliative operation and radiotherapy can be overcome by the selective chemotherapy. The Cancer-Chemotherapy-Sensitivity-Test is a valuable tool in selecting the most effective cytostatic drug. The resistance of the malignant tumour against the carcinostatic agent is no more a therapeutical problem when the sensitivity test is performed.