CeU 01

THE PREVALENCE OF HUMAN PAPILLOMAVIRUS (HPV) DNA IN INVASIVE CERVICAL CARCINOMA OF DIFFERENT CLINICAL STAGES DEPENDENT ON HISTOLOGIC TYPE AND GRADE OF DIFFERENTIATION
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Human papilloma virus is associated with a variety of human genital tumours. The HPV types 6 and 11 are mainly found in benign lesions while HPV 16 and 18 are more prevalent in carcinomas in situ and invasive carcinoma of cervix, vulva and penis. Up to now it is unclear whether a correlation between the prevalence and type of HPV on the one hand and the histologic type, grade of differentiation and clinical stage of the tumour on the other hand exists. We tested 76 clinically and histologically uniformly defined invasive carcinomas and 15 normal tissues of the uterus for the prevalence of HPV DNA by southern blot hybridization. 46/55 (83.5%) invasive squamous cell carcinomas of the cervix contained HPV 16, 2/55 (3.5%) not yet defined HPV DNA and 7/55 (13%) were negative for HPV (sensitivity greater than one genome copy HPV DNA per cell). 8/8 tumours of the clinical stage Ia/b, 14/16 stage IIa/b, 19/25 stage III and 5/6 stage IV tumours were HPV 16 positive. In 36% of the stage I/II versus 50% of the stage III/IV lesions more than 10 copies HPV DNA per cell were found. 3/6 adenocarcinomas of the cervix but 0/15 adenocarcinomas of the corpus uteri contained HPV 16. In none of 15 corresponding normal tissues of HPV positive tumour patients HPV DNA could be identified. Only 3/6 highly differentiated squamous cell carcinomas were HPV positive compared to 24/27 (89%) lesions with a medium and 21/22 (95%) lesions with a low grade of differentiation.

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CeU 02

DIGNITY OF CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) USING A DNA CYTOPHOTOMETRY METHOD IN HPV-INFECTIONS
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The association of human papilloma viruses (HPV) types 16 and 18 with cervical carcinomas and HPV types 6 and 11 with benign genital lesions as well as the presence of both types in cervical dysplasia suggests a distinction between high risk and low risk dysplasia. This hypothesis was studied in our investigations using the results from 500 patients examined by DNA cytophotometry and by comparing the isolated viruses with the histological and cytological changes. A marked increase of HPV infections could be established among patients with cervical intraepithelial neoplasia (CIN) compared to control group. The rate of HPV 6/11 infections primarily rose among patients with slight to moderate dysplasia, while the HPV 16/18 infections increased in cases of marked dysplasia, carcinoma in situ and cervical carcinoma. Cytophotometric DNA measurements were additionally made in 30 cases of slight to moderate dysplasia identified as HPV 6/11 or 16/18 infections. Three types of histogram defined by the position of the stem-line could be established:

- 1) histogram with an aneuploid stem-line in HPV 16/18 infections
- 2) histogram with euploid-polyploid stem-line in HPV 6/11 infections
- 3) histogram without any stem-line

The cytophotometric findings support the hypothesis that CIN containing HPV 16/18 thus have to be considered precancerous lesions with a high risk and lesions related to HPV 6/11 with a low risk of progressing to cancer.

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CeU 03

EARLY DIAGNOSIS OF MALIGNANCY IN CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) WITH INTERACTIVE DNA-CYTOMETRY
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Dysplasias of the squamous epithelium of the uterine cervix represent a "diagnostic urgency" in cytological and histological diagnosis as they do not allow to distinguish between precancerous and non precancerous lesions unequivocally. The clinical outcome of dysplastic lesions can usually not be foreseen from morphological aspects. A non morphological method is therefore requested that can predict the malignant or benign behavior of individual dysplastic lesions using the same cells or tissues that yielded the diagnosis of dysplasia. Such a method is the interactive nuclear-DNA-cytometry on Feulgen-stained smears. This procedure was used for the detection of malignancy in smears from 70 cervical intraepithelial neoplasias (dysplasias), 13 doubtful cases and in seven invasive carcinomas. DNA-measurements were performed with a TV-image analysis system combined with an automatic microscope and with a scanning microphotometer. The data were computed by an algorithm for a DNA-cytophotometric diagnosis of malignancy. Malignant diagnoses were verified histologically. No false positive diagnosis occurred in 183 benign smears and one false negative diagnosis in 76 histologically proven squamous cell carcinomas resulting in a specificity of 100% and a sensitivity of 99%. The sensitivity for the detection of histologic evident malignancy in cytologically dysplastic or doubtful cases amounted to 97%. In 17% of cytologically doubtful or dysplastic cases the malignant DNA-diagnosis could not yet be affirmed by histological investigation. Thus interactive DNA-cytometry is able to detect malignancy in smears from cervical intraepithelial neoplasias (dysplasias) with high sensitivity. Using automated Feulgen staining and rapid interactive DNA-image cytometry with a TV-system and an automated microscope the whole diagnostic procedure becomes easier and quicker and may be introduced in the routine laboratory.

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CeU 04

PERIAORTIC STAGING IN ENDOMETRIAL AND CERVICAL CANCER - RISK VERSUS BENEFIT
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A review of the studies reported indicates that exploratory laparotomy for staging purposes including pelvic and paraaortic lymphadenectomy contributes significantly to the exact evaluation of gynecologic cancers. Patients who have extension of their disease beyond the pelvis have a prognosis dependent on the extent of this spread. Survival rates range from 50% for those patients with spread to one group of nodes unilaterally, to virtually nil for patients with macroscopic spread to the paraaortic nodes (B.C. Ward, Brit. Med. J. 290, 1301, 1985).

73 patients underwent staging laparotomy for operable cervical cancer, 31 of this group had additional paraaortic lymphadenectomy without increased complication rates or postoperative morbidity. 39 patients had operative staging of endometrial cancer. Patients with extrapelvic spread were considered as candidates for systemic treatment. Since intra- and postoperative complications are low, it might be suggested that continued studies on improved local control and treatment of systemic disease need to be carried out as part of a pretreatment surgical staging protocol (H.W. Jones, in: Gynecologic Oncology - Controversies in Cancer Treatment, Ed. S.C. Ballon, Hall, Boston 1981).

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