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EFFECT OF BCNU ON XENOGRAFTS OF A MIXED SENSITIVE AND RESISTANT HUMAN SMALL CELL LUNG CANCER IN NUDE MICE

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In vitro established human small cell lung cancer cell lines of a BCNU sensitive (592) and a resistant (NYH) tumor were used to produce solid tumors in nude mice. Mixtures of 592:NYH = 9:1 and 1:1 were inoculated s.c. After 2 weeks of tumor growth, the mice were randomised to treatment with BCNU 40 mg/kg i.p. or no treatment. During the experiment, response and changes in the relative 592:NYH proportions were monitored by growth curves and by fine-needle tumor aspirations with flow cytometric DNA analysis by which the two cell lines were distinguishable. A significant response was demonstrated in the 9:1 mixed tumors in which only 592 cells were detectable at treatment start. The response was short compared with tumors containing only 592. At relapse, only NYH was detected. The 1:1 mixed tumors did not respond significantly to BCNU although 592 disappeared. These results indicate that resistant and not detectable (silent) subpopulations in heterogeneous tumors may be responsible for relapse, and that the proportion of resistant cells may determine the magnitude of the clinical response to cytostatic treatment.

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TREATMENT AND PROGNOSIS OF METASTATIC EPIDURAL SPINAL CORD COMPRESSION

F. Bach, P.S. Sørensen, S.E. Børgesen, K. Rohde, B. Rasmussen, T.B. Rasmussen, P. Stjernholm, B. H. Larsen, N. Agerlin and F. Gjerris. Departments of Oncology, University Hospital Herlev and the Finsen Institute. Departments of Neurology and Neurosurgery, Rigshospitalet, Glostrup and Hvidovre Hospitals, Copenhagen. We reviewed all medical records of patients treated for metastatic spinal cord compression, in the eastern part of Denmark, from 1979 through 1985. The series comprised 398 cases with carcinoma of the prostate, lung, breast and kidney, as the most frequent malignancies, accounting for 61%. The outcome of treatment was evaluated from changes in neurological deficits and sphincter function, and depended primarily on the patients condition, at the time of diagnosis. Of the patients who were able to walk, before start of treatment, 79% remained ambulatory, whereas only 16% of the paraplegic patients regained walking ability. Patients treated with laminectomy followed by radiotherapy (24%) had a significant better response ($p=0.002$), than patients treated with radiotherapy alone (41%) or laminectomy alone (27%). Furthermore they had a longer survival, however this may reflect a less extensive stage of the disease. The findings which favor the treatment combination of laminectomy and subsequent radiotherapy may call for prospective randomized studies.

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ENDOGENOUS NITROSATION IN RELATION TO NITRATE EXPOSURE FROM DRINKING WATER AND DIET IN A DANISH RURAL POPULATION.

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Increasing levels of nitrate in drinking water in Denmark is of concern due to the possibility of an associated increase in long-term exposure to endogenously formed carcinogenic N-nitroso compounds.

Excretion of N-nitroso-L-proline in 12 h overnight urine after intake of 500 mg L-proline is used to quantify the rate of endogenous formation of N-nitroso compounds in 285 individuals. Nitrate intake during the day before urine collection is measured in a 24 h duplicate diet sample. A qualitative description of the composition of the diet and a questionnaire on smoking and other background variables is used.

The crude association between nitrate concentration in drinking water and rate of nitrosation is positive but not statistically significant. Total nitrate intake and smoking are the most important determinants of endogenous nitrosation. In non-smokers, nitrosation is strongly associated with increasing nitrate intake. Smokers have increased nitrosation which does not depend on nitrate intake.

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EVOLUTION OF CLONAL HETEROGENEITY OF ANEUPLOID CELL POPULATIONS IN CARCINOMA IN SITU OF THE BLADDER INVESTIGATED BY FLOW CYTOMETRY.

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Carcinoma in situ of the bladder (CIS-B) frequently progresses into invasive cancer after an unpredictable period of latency. Mechanisms behind this process are poorly understood. By flow cytometric (FCM) DNA-ploidy analysis small mucosal biopsies may be analyzed using a simple preparation technique with nuclei isolation by a detergent and quantitative DNA staining with the fluorochrome ethidium bromide.

In CIS-B multiple biopsies have shown frequent heterogeneity with up to 6 different aneuploid cell populations in one bladder, each population having its own, distinct DNA content. In a consecutive series of 13 bladders the average number of aneuploid cell populations per bladder was 2.2.

Repeated biopsies and bladder washings from patients controlled for CIS-B are analyzed for eventual evolution of abnormal cell clones and invasive cancer. Preliminary results from the first year of the investigation (1987) indicate a great variability with time in ploidy and number of cell populations.