

cancer shows the well-known urban-rural variation, except for Finnish males, where the incidence rates are fairly constant throughout the country. All cancers showed a limited variation in incidence, with a ratio of incidence rates between the regions with highest and lowest of 1.7. For both men and women the high incidence area is Copenhagen, but for men the lowest incidences are found in rural Sweden and Norway, and for women in rural Finland.

THE IMPORTANCE OF TUMOR OXYGENATION STATUS FOR ANTINEOPLASTIC THERAPY. C.Grau, J.C.Lindgaard & J.Overgaard. The Danish Cancer Society, Nørrebrogade 44, DK-8000 Århus C, Denmark.

The heterogeneity of solid tumors due to differences in intratumoral oxygenation status is believed to influence the effect of several cancer treatment modalities. Based on results from a clamped tumor control assay using a C3H mouse mammary carcinoma *in vivo*, the effect of various antineoplastic agent on aerobic and hypoxic cells was determined. The agents could be divided into three categories:

- (1) preferential activity against aerobic cells: Cisplatinum, Bleomycin, Methotrexate, X-rays.
- (2) preferential activity against hypoxic cells: Hyperthermia, Etoposide, Misonidazole.
- (3) activity against both cell types: Mitomycin C, Cyclophosphamide, Adriamycin, Vincristine.

The significant killing of hypoxic cells observed for agents in category (2) and (3) correlated with the ability of these agents to cause a significant enhancement in radiation response. The drugs in class (1) did not improve the radiation response. We conclude that tumor hypoxia might be an important factor in the development of drug resistance in solid tumors. The specific toxicity of antineoplastic agents on aerobic and hypoxic cells needs to be considered, especially in the agents are used in combination with radiotherapy.

HETEROGENEITY IN CERVICAL CANCER. B.Norrild, A.Sebbelov, A.Iversen.

Heterogeneity can be considered at several levels - the microscopic or the molecular level. Cancers with a possible viral etiology could be considered as one group of cancers with an internal heterogeneity as virusproducts can be demonstrated in certain cells in the tumor but not in all cells. Cervical cancer which at present is considered to be caused by human papilloma virus (HPV) is one example where heterogeneity apparently do exist. Between 60% and 80% of the tumors contain HPV DNA analysed by the Southern Blot test. In situ hybridi-

zation on paraffin sections demonstrate HPV-DNA in selected cells within a premalignant lesion. Is this heterogeneity true or is it a result of lack of sensitivity of the tests used? Data from our studies will be discussed in relation to application of the Polymerase Chain Reaction to samples scored negative in the "standard" tests used.

AMPLIFICATION OF *myc* FAMILY ONCOGENES IN TUMOR BIOPSIES FROM PATIENTS WITH SCLC. K.Rygaard, G.D.Sorenson & M.Spang-Thomsen. University Institute of Pathological Anatomy, Copenhagen and Dartmouth Medical School, Hanover, New Hampshire, USA.

Activation of oncogenes is found in a variety of human malignancies, and amplification of members of the *myc* family is often found in small cell lung cancer (SCLC). In this study the level of amplification of selected oncogenes was determined in biopsies of 9 metastatic lesions from patients with SCLC. The tumors CPH 136A and 136B were from the same patient before and after single drug VM-26 chemotherapy. DNA was extracted by standard methods and digested with restriction endonucleases. Ten micrograms per lane was electrophoresed in 0.8% agarose gels and transferred to nylon membranes. Southern blots were probed with oligolabeled oncogene fragments. One tumor (CPH 160) had approx. 8-fold amplification of *c-myc*. Two tumors (CPH 124 and 136A) had approx. 10-fold amplification of the 10 kb *L-myc* band. No amplification was seen of *N-myc*, *c-myb*, *N-ras* or *H-ras*. Thus, amplification of one of the members of the *myc* oncogene family was found in 3 out of 9 tumor biopsies. This figure is comparable with the high amplification frequency of *myc* oncogenes reported for SCLC.

ISOLATION AND CHARACTERIZATION OF A HIGH AND LOW TUMORIGENIC SUBLINE OF HUMAN T24 BLADDER CARCINOMA CELLS.

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Two sublines of the T24 human urinary bladder carcinoma cell line, T24A and T24B, which differ in tumorigenicity has been isolated. The sublines differed in morphology and in growth rate *in vitro* and *in vivo*. T24A had a 5 times delayed tumor take after subcutaneous injection and at the same time a higher expression of HLA than T24B. Following intravenous injections in the tail vein of nude mice lung metastases were only produced by T24B. No differences were seen with respect to the type of invasion into mouse heart tissue *in vitro*, but the intercellular adhesion was tighter between the T24A cells than between T24B