Abstracts of Theses from the Nordic Countries

Abstracts of Nordic theses on oncologic subjects are published under this heading. The full theses are as a rule published by the universities or as supplements to different journals. They can usually be obtained after contact with the author.

Cancer risks among agricultural workers in Sweden
Cohort studies based on the Swedish Cancer-Environment Register

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The aim of this dissertation was to study cancer risks and their time-related trends among Swedish agricultural workers. The cohort of agricultural workers was defined according to registered economic activity in the 1960 population and housing census and was followed up in the period 1961–1979 in the Cancer-Environment Register. The reference cohort comprised persons gainfully employed in economic activities other than agriculture or forestry. The overall cancer risk was lower among agricultural workers. The lowest estimated relative cancer risks were found for respiratory organs, liver (primary) and biliary passages, urinary organs (incl. renal pelvis), oesophagus and malignant melanoma of skin in trunk and limbs. Estimated relative risks higher than unity were observed for cancer of the lip, malignant melanoma and skin carcinoma of the head-neck region, multiple myeloma and cancer of the stomach. For soft-tissue sarcoma the estimated relative risk was not higher than unity and no time-related trend was observed. During the studied period the estimated relative cancer risk increased significantly ($p<0.01$) for all sites together and for certain specific sites as liver (primary), prostate, other male genital organs and urinary organs. For most of these sites, the relative risk remained lower than increased towards unity. (February, 1986)

DNA ploidy and DNA replication as predictors of relapse-free survival and response to therapy
Studies with special reference to breast cancer

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The significance of DNA ploidy and DNA replication as predictors of five-year relapse-free survival in 360 breast cancer patients was investigated and compared with established prognostic variables. For the assessment of DNA pattern Feulgen-acriflavine-SO_2 imprint specimens were analyzed by means of static cytometry in 150 patients. Two hundred and ten patients were included in a second study where the DNA measurements were performed by both flow cytometry and static cytometry. The concordance of measurements of DNA ploidy and fraction of S-phase cells as assessed by means of flow cytometry and static cytometry was explored in 332 mammary carcinomas. Retinoid receptor content in 148 human mammary carcinomas was investigated and correlated to estrogen receptor level, DNA pattern, and clinical outcome. The change of DNA replication during therapy was investigated in 24 treatment courses in 12 patients. Significant prognostic predictors of five-year relapse-free survival were axillary lymph node status, clinical stage, proliferative index, and estrogen receptor status while DNA ploidy gave no independent prognostic information. Flow cytometry and static cytometry gave similar estimates of DNA ploidy and S-phase fraction. In malignant lymphomas, successful tumor therapy was accompanid by rapid changes in DNA replication.

The present results show that there are objectively measurable cell parameters that add prognostic information to established clinical parameters. It is reasonable to assume that the possibilities offered by the analysis of such cell parameters would provide valuable information for the planning of individualized tumor therapy. (March, 1986)

Studies on the mechanism of daunorubicin-mediated toxicity in cultured heart cells, with special reference to free radicals

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Cultures of isolated and beating heart cells from neonatal rats were established using a collagenase based protease mixture for the disaggregation of the heart tissue. As judged by the short time period required for the cells to attach to petri dishes and start beating, this protease mixture gave a high yield of viable heart cells with much less damage than trypsin-based preparations previously utilized. These beating cells were then utilized in experiments designed to study the mechanism(s) of daunorubicin-mediated cardiotoxicity. Among the enzyme activities investigated, glutathione transferase and DT-diaphorase were induced in the cultured heart cells after daunorubicin treatment. Glutathione transferase catalyzes the formation of glutathione conjugates, while DT-diaphorase may reduce quinones, in a two electron reaction, to the relatively more stable hydroquinones and in this way compete with one electron reductases. Treatment of the cultured cells with dicoumarol—a potent and specific inhibitor of DT diaphorase—increased the sensitivity of the cells towards daunorubicin. The cyanide-insensitive respiration of the cultured cells was dramatically increased after addition of daunorubicin to the growth medium, indicating oxygen-derived free radical formation. These free radicals are thought to be generated after one electron reduction of the quinone group to daunorubicin semiquinones by various flavin-containing reductases and subsequent autooxidation of the semiquinones. Furthermore, the concentration of glutathione in the cells was gradually decreased, which resulted in cell damage as judged by the release of the cytosolic enzyme lactate dehydrogenase. Interestingly, only the cytosolic pool of cellular glutathione was decreased by daunorubicin while the mitochondrial pool was essentially unaffected, suggesting that cell damage was related to an alteration of cytosolic rather than mitochondrial glutathione. Release of glutathione to the surrounding medium was concluded to be unrelated to the toxicity of daunorubicin. Addition of 0.5 mmol hydrogen peroxide potentiated the effects of daunorubicin indicating that the degradation of H_2O_2 is of great importance in the case of daunorubicin-mediated toxicity. Free radical scavengers and antioxidants of various kinds offered little or no protection, while the thiol substance dithiothreitol was the most potent protector of the cells. It is concluded that a perturbation of the glutathione status mediated through the action of oxygen-related free radicals, formed after daunorubicin reduction and autoxidation, is the primary cause of daunorubicin-mediated cardiotoxicity. (March, 1986)

Bone tissue response to irradiation and treatment model of mandibular irradiation injury
An experimental and clinical study

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The present study was conducted on bone tissue responses to irradiation towards a treatment model of mandibular irradiation injury by comparing the results of experimental observations of

irradiation effects on rabbit hind legs and rat mandibular bones with clinical observations of irradiation effects on the human mandible. The main results of the study were as follows: 1) Bone marrow hemorrhage, eosinophilia and incipient oedema were encountered in the rabbit leg one day after a single irradiation dose. Edema and fibrosis were the salient features after five weeks, while both regenerative and fibrotic changes predominated eleven weeks after irradiation. The changes were the more extensive the greater the irradiation dose was. Empty lacunae as a sign of cell damage in cortical bone already appeared on the first day after irradiation; this effect reached its maximum when the dose was 20 Gy or more. 2) Bone marrow and subcutaneous tissue pO_2 and pCO_2 were measured by means of implanted Silastic tonometers in irradiated and non-irradiated rabbit hind legs. Single dose irradiation was followed by a rapid, dose dependent decrease of marrow pO_2. The corresponding effect on pCO_2 was weaker and appeared later. The response to hyperoxia in the bone marrow became weaker when the irradiation dose increased. Less significant was the response of CO_2 tension to hyperoxia. O_2 and CO_2 tensions were recovered after single dose irradiation both in subcutaneous tissue and in bone marrow, but the reduction was less in bone marrow. During the twelve-week observation period clearly better recovery in tissue gas tensions was observed in subcutaneous tissue than in bone marrow. 3) Non-irradiated periosteal grafts on irradiated bone cavities in the rabbit tibia induced more rapid and intense mature bone formation than irradiated periosteal grafts. The irradiated periosteum, even after a single dose of 20 Gy, had some osteogenetic capacity. The alkaline phosphatase content was lowered eight weeks after surgery in irradiated legs but clearly exceeded control values twelve weeks after surgery indicating new bone formation. Lysosomal enzyme DAP II contents were increased in all irradiated specimens as a sign of disturbed bone formation. 4) The tissue concentrations of acid phosphatase, cytochrome oxidase, lactate dehydrogenase isocitrate dehydrogenase, glucose-6-phosphate dehydrogenase and succinate dehydrogenase in the immediate postirradiation period showed a greater increase in activity in the cut lines of the irradiated rat mandibles than in those of the non-irradiated mandibles. The activity increased with dose and time over the 24-hour observation period. 5) After irradiation of the healthy mandible, slight but significant elevations of uptake levels were detectable by computerized analysis of $^{99}Tc^{m}$ MDP scintigraphy. The scintigraphy may be used to predict whether osteoradionecrosis will develop in the irradiated mandible. 6) By morphometric methods a decrease in the number of trabeculae and a relative increase in the amount of marrow space were shown to occur during radiation therapy. The changes were reversible, which signifies the recovery of bone after irradiation at therapeutic doses. 7) The clinical trials with tibial periosteal grafting combined with surgical eradication of the focus and auxiliary hyperbaric oxygenation and antimicrobic therapy in mandibular osteoradionecrosis and osteomyelitis showed clinical recovery, which was promising enough with a view to extended use of the method in the management of these severe diseases.

(April, 1985)

The European Association for Cancer Education

At the 14th International Cancer Congress (Budapest, October 1986) it was decided to establish the European Association for Cancer Education. The official foundation of EACE took place on 28 January 1987.

The members of the Executive Council are G. S. Ingimarsson (President, Reykjavik), W. Bender (Secretary, Groningen), J. Einhorn (Stockholm), E. M. L. Haagedoorn (Groningen), R. M. Harden (Dundee) and C. D. Sherman (New York).

The EACE wants to be a forum for members to exchange ideas and materials concerning cancer education, including educational research. The aim is to bring together people from different professional groups or disciplines who in different ways are involved in the educational aspects of cancer. One tool to reach this goal will be the Annual Meeting which will be held in alternating countries throughout Europe.

In fighting cancer, education is one of the keys. If you are interested in the EACE, please write to the Secretary; he will be happy to keep you informed on ongoing activities.

Members of the European Association for Cancer Education receive the Journal of Cancer Education for half the price as part of their dues. The membership fee is 55 ECU (the Journal of Cancer Education included). Institutions may subscribe to a collective membership; in that case the fee can be reduced as decided upon by the Executive Council.

Further information may be obtained from the Secretary of the EACE, Dr W. Bender, Centre of Medical Education Research and Development, Bloemsingel 1, 9713 BZ Groningen, The Netherlands.