Abstracts of Theses from the Scandinavian Countries

Abstracts of Scandinavian 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.

Intraurothelial neoplasia of the urinary bladder—DNA characteristics and prognostic aspects

U. NORMING

Department of Urology, Södersjukhuset, and Department of Medical Radiobiology, Karolinska Institute, Stockholm, Sweden

In a study of 290 patients with untreated transitional carcinoma of the bladder the DNA ploidy of selected site biopsies, as measured by flow cytometry DNA analysis, was related to stage, grade and ploidy of the tumor and to histopathology of the grossly normal mucosa. Aneuploidy as well as histopathological abnormalities of the mucosa occurred almost exclusively in aneuploid tumors of grade 3, and at a significantly higher frequency in superficial (Ta/T1) than in muscle invasive ($\geq$T2) tumors of grade 3. The modal DNA values of mucosa were closely related to those of the tumors. It was concluded that, in addition to gross chromosomal aberrations, the evolution from the intraurothelial lesion to a gross neoplasm is dependent on further changes of the phenotype. Aneuploidy was detected in 76, 41 and 10% respectively, of mucosal biopsies classified as carcinoma in situ, atypia of lower degree and normal. Gross chromosomal aberrations may thus appear at an early stage of the tumor development and before changes detected by morphology.

In a series of 71 patients with newly detected stage Ta/T1 grade 3 bladder carcinoma the characteristics of tumors and mucosa of the 47 patients who were not primarily cystectomized were related to tumor progression ($\geq$T2). Aneuploidy and morphological abnormalities (carcinoma in situ or atypia) in mucosal biopsies at 12 months after diagnosis were the only factors predicting tumor progression ($p = 0.001$ and $p = 0.045$ respectively). In stepwise regression analysis morphology was, however, shown not to add further prognostic information when the results of flow cytometry were given. In conclusion, tumor progression is correlated to the existence of concomitant neoplastic intra-urothelial changes. It was suggested that DNA analysis should be performed in addition to morphological evaluation of the mucosa at diagnosis as well as during follow-up.

In a study of 63 patients with primary grade 3 carcinoma in situ the DNA profiles were related to progression and outcome of therapy. The existence of multiple aneuploid cell populations at diagnosis or the development of such a DNA profile, indicated a high risk of progression ($\geq$T1) whereas patients with one aneuploid cell population were at low risk. Of the 37 patients who manifested progression, 34 had multiple aneuploid cell populations. Persistence of this DNA profile in spite of topical treatment as well as development from one to several aneuploid cell populations during the course of such therapy, indicate a need for radical treatment. After progression, cystectomy seemed to be the only possible cure, since irradiation therapy failed in all cases.

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Proliferation associated nuclear antigens—A flow cytometric study with special reference to proliferating cell nuclear antigen (PCNA) and Ki-67 antigen

G. LANDBERG

Department of Pathology, University of Umeå, S-901 87 Umeå, Sweden

Cell proliferation can be assessed using various different methods such as DNA histogram analysis, determination of incorporated nucleic acid precursors or evaluation of growth related antigens. In the present study the coordinated expression of proliferating cell nuclear antigen (PCNA) and Ki-67 antigen was investigated by flow cytometry in hematopoietic cells. Using this technique five distinct cell populations, representing G0, G1, S, G2 and M respectively, could be demonstrated in a mixture of proliferating and resting cells. In human lymphoma cells the fractions of cells positive for a human anti-PCNA serum and the moab Ki-67 were strongly correlated to each other as well as the number of S-phase cells determined by DNA histogram analysis. In mitogen-stimulated peripheral blood lymphocytes the recruitment of cells into the cycle from a resting stage could be determined due to a difference in Ki-67 expression in early PCNA positive S-phase cells entering the cell cycle compared with continuously cycling cells. This cell cycle parameter can give additional information concerning tumor growth and may be important to study, especially with respect to the effect of chemotherapy.

The expression of different proliferation associated nuclear antigens was furthermore analysed using a washless double-staining method and flow cytometry. The two-step procedure, which can be performed on low cell numbers, was found to be applicable to a number of nuclear antigens (PCNA, Ki-67, p150, MPM-2, fibrillarin). However, for PCNA the detectability was dependent on the type of antibody used.

The usefulness of anti-PCNA monoclonal antibodies as S-phase probes in flow cytometric analysis was evaluated after various fixation procedures. The monoclonal antibody PC10 was the only antibody which acted as an S-phase marker in cell lines and in human hematopoietic tumor cells using a newly developed detergent extraction/fixation method. On the other hand PC10 recognized all actively cycling cells using alternative fixation procedures, a feature also observed for the monoclonal antibodies 19A2 and TOB7. The variation in reactivity found for the monoclonal antibodies could be explained by differences in epitope recognition. Using completion analysis with synthetic peptides encoding the entire PCNA amino acid sequence, five monoclonal antibodies were shown to react with the same protein region whereas one monoclonal antibody recognized a separate region of the protein. The immunodominant epitope was studied in detail using Ala-substituted peptides and microheterogeneity could be demonstrated within this region concerning recognition sites for different monoclonal antibodies.

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Biological effects of high energy radiation and ultra high dose rates

B. ZACKRISSON

Department of Oncology, University of Umeå, S-901 85 Umeå, Sweden

Recently a powerful electron accelerator, 50 MeV race-track microtron, has been taken into clinical use. This gives the opportunity to treat patients with higher x-ray and electron energies than before. Furthermore, treatments can be performed where the entire fractional dose can be delivered in parts of a second.

The relative biological effectiveness (RBE) of high energy photons (up to 50 MV) was studied in vitro and in vivo. Oxygen enhancement ratio (OER) of 50 MV photons and RBE of 50 MeV electrons were investigated in vitro. Single-fraction experiments, in vitro, using V-79 Chinese hamster fibroblasts showed an RBE for 50 MV x-rays of approximately 1.1 at surviving fraction 0.01, with reference to the response to 4 MV x-rays. No significant difference in OER could be demonstrated. Fractionation experiments were carried out to establish the RBE at the clinically relevant dose level, 2 Gy. The RBE calculated for the 2 Gy/fraction experiments was 1.17. The RBEs for 20 MV x-rays and 50 MeV electrons were equal to one. In order to investigate the validity of these results, the jejunal crypt microcolony assay in mice was used to determine the RBE of 50 MV x-rays. The RBE for 50 MV x-rays in this case was estimated to be 1.06 at crypt surviving fraction 0.1. Photonuclear processes are proposed as one possible explanation to the higher RBE for 50 MV x-rays.

Several studies of biological response to ionizing radiation of high absorbed dose rates have been performed, often with conflicting results. With the aim of investigating whether a difference in effect between irradiation at high dose rates and at conventional dose rates could be verified, pulsed 50 MeV electrons from a clinical accelerator were used for experiments with ultra-high dose rates (mean dose rate: 3.8×10^2 Gy/s) in comparison to conventional (mean dose rate: 9.6×10^{-2} Gy/s). V-79 cells were irradiated in vitro under both oxic and anoxic conditions. No significant difference in relative biological effectiveness (RBE) or oxygen enhancement ratio (OER) was observed for ultra high dose rates compared to conventional dose rates.

A central issue in clinical radiobiological research is the prediction of responses to different radiation qualities. The choice of cell survival and dose response model greatly influences the results. In this context the relationship between theory and model is emphasized. Generally, the interpretations of experimental data are dependent on the model. Cell survival models are systematized with respect to their relations to radiobiological theories of cell kill. The growing knowledge of biological, physical, and chemical mechanisms is reflected in the formulation of new models. This study shows that recent modelling has been more oriented towards the stochastic fluctuations connected to radiation energy deposition. This implies that the traditional cell survival models ought to be complemented by models of stochastic energy deposition processes at the intracellular level.

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Viral hepatitis and chronic liver disease in Ethiopia: Epidemiological and clinical aspects

E. TSEGA

From the Department of Internal Medicine, Faculty of Medicine; Addis Ababa University, Ethiopia; in collaboration with Department of Microbiology, section of Virology, Malmo General Hospital, Lund University, Sweden

The epidemiological and clinical aspects of viral hepatitis and chronic liver disease in Ethiopia were studied. Population surveys involving rural and urban dwellers, blood donors, hospital staff, patients with acute viral hepatitis and chronic liver disease have shown that HAV, HBV, HDV and NANB (including HCV and HEV) are endemic. Hepatitis A virus infection occurred asymptomatically during childhood, anti-HAV-IgG was detected in all subjects over 15 years of age and infection was associated with low socioeconomic status. Hepatitis B virus infection occurred early in life and gradually increased with age to involve about 80% of adults. The HBsAg carrier state varied between 5% and 11% depending on age. There was a tendency for early conversion of HBeAG to anti-HBe. Horizontal transmission within families was more important than vertical transmission, and some traditional practices appeared to be risk factors. Anti-delta or anti-HDV occurred in 3% of 81 healthy HBsAg carriers as compared to 25% of 92 carrier patients with chronic liver disease. Anti-HCV, determined by ELISA, was positive in 73 (11%) of 659 healthy subjects, 12 (10%) of 126 patients with acute viral hepatitis and 148 (70%) patients with chronic liver disease. Infection with HEV was responsible for a mild and self-limited epidemic hepatitis among 423 military men in northern Ethiopia. Hepatitis E virus was a common (33%) cause of acute sporadic viral hepatitis and its occurrence in pregnancy was associated with high maternal and perinatal morbidity and mortality. Chronic liver disease (chronic hepatitis, cirrhosis and hepatocellular carcinoma) are common and 83% of these patients had HBV markers and 38% anti-HCV. Epidemiological and clinical findings, the high prevalence of HBV and HCV infections suggest an aetiological association. Trials of two different hepatitis B vaccines, administered alone or concurrently with the Expanded Programme on Immunization (EPI) were found safe and immunogenic in newborns and in children 2–14 years old. Immediate implementation of mass vaccination of newborns with HBV vaccine, integrated with the EPI, is recommended. While prevention of HCV infection requires knowledge of modes of transmission and production of effective vaccine, there is an urgent need for socioeconomic improvement and vigorous public health education to control HAV and HEV infections.

November 1991

Ischaemic treatment of liver cancer

S. SJÖVALL

From the Department of Surgery, University Hospital, S-221 85 Lund, Sweden

Liver cancer untreated leads rapidly to death. The ischaemic treatment of the liver has opened new palliative possibilities for patients with irresectable liver malignancies. The effect of ischaemic treatment was studied in the experimental model in the rat concerning the liver metabolic responses, the liver tumour growth, the liver tumour blood flow, and efficiency of a cytostatic agent and lipoidol, and the unstructural changes. In addition, the consequences of hepatic dearterialisation on glucose tolerance and insulin secretion were studied in patients with liver malignancies.

Hepatic dearterialisation induces hyperglycaemia, hyperinsulinaemia, and hypoglucagonaemia, but impairs the argenine-induced increase in insulin secretion. Further, the liver glycogen stores are decreased, probably due to an exaggerated glycogenolysis.

Hepatic dearterialisation reduces the hepatic activity of hepatic lipase probably due to an inhibition of de novo enzyme synthesis, reduces the oxidative capacity of the mitochondria, and inhibits the microsomal enzyme cytochrome (P_{450}) activity.

Hepatic artery or portal vein occlusion reduces the tumour growth rate, and causes similar decrease of blood flow in both normal and tumour tissue. In both tissues the decrease upon occlusion of the portal vein was more pronounced than upon occlusion of the hepatic artery.

The retarding effect of intermittent hepatic artery occlusion on tumour growth was not significantly potentiated with the additional treatment of MMC and lipoidol.

A gradual development of ultrastructural changes in the liver tissue started after 30 min of ischaemia. No difference was observed between hepatic arterial and portal venous ischaemia. Reflow adverses the morphological changes caused by ischaemia.

November 1991

Prognosis and diagnosis of non-Hodgkin lymphomas—the role of proliferation associated parameters and magnetic resonance imaging

S. REHN

From the Department of Oncology, University of Uppsala, Akademiska sjukhuset, S-751 85 Uppsala, Sweden

The non-Hodgkin lymphomas (NHL) are tumors derived from different differentiation stages of cells in the immune system. The two major prognostic groups of NHL, high-grade and low-grade, are very different in their clinical behaviour, response to treatment and prognosis. Even within these two main groups, there exists great heterogeneity. It is important not only to differ between these two groups but also to better predict the prognosis for each individual patient at the time of diagnosis in order to provide the best possible treatment. This work has focused its attention on the ability of proliferation-associated parameters and MRI to predict prognosis and prognostic grade.

High values for the fraction of tumour cells synthesizing DNA (S-phase fraction) indicate rapid tumour growth and have been shown to entail a poor prognosis in short-term follow-ups for the entire patient material and after prolonged follow-up time for high-grade NHL.

Serum deoxythymidine kinase (S-TK), which probably reflects both the extent of proliferation and the tumour mass, had the strongest prognostic value in all groups. Another proliferation-associated parameter, the fraction of dividing cells (mitosis), had prognostic value independent of S-TK, especially in low-grade NHL.

Lymphatic tissues have identical MRI characteristics as long as cellularity remains the same. MRI does not enable the identification of the degree of proliferation in tumour-involved tissues. In tissues such as bone marrow, which normally contains varying amounts of fat, the extent of cell infiltration can be detected and calculated from MRI data. Localized tumour infiltration of the bone marrow can therefore be suspected. Tumour involvement of the spleen and liver could only be detected if there had occurred an involvement by different tissue components such as fibrosis, necrosis, oedema or an accumulation of iron.

In involved lymph nodes, high-grade NHL often displayed an inhomogeneous appearance probably due to necrosis. A subjective evaluation of the homogeneous or inhomogeneous appearance at MRI could distinguish well between low- and high-grade NHL. Inhomogeneities also entailed a poor prognosis. A method of measuring the degree of inhomogeneity was developed and improved the sensitivity of detecting high-grade malignancies and also improved the prognostic strength of MRI.

November 1991

Uterine leiomyoma cytogenetics

M. NILBERT

From the Department of Clinical Genetics, University Hospital, S-221 85 Lund, Sweden

Cytogenetic analyses were performed on 382 uterine leiomyomas from 263 patients. Clonal chromosome aberrations were detected in 71 tumors, normal karyotypes in 240, and 71 tumors yielded an insuffiicent number of mitoses for analysis. Cytogenic groups characterized by primary chromosome abnormalities including der(6p) (10 tumors), del(7q) (14 tumors), trisomy 12 (11 tumors), t(12; 14) (11 tumors), der(12q) (3 tumors), and der(14q) (3 tumors), were identified. Secondary karyotypic rearrangements, which reflect clonal evolution, were observed in one third of the tumors with primary chromosome anomalies. The secondary abnormalities often included ring formation and various changes of chromosomes 1, 13, and 22. Three leiomyomas had massive numerical as well as structural changes. All three were large (9–10 cm) and showed histopathologic features indicative of atypia; increased cellularity, enlarged hyperchromatic nuclei, and an increased number of mitoses.

Multiple (2–8) leiomyomas from the same uterus were studied from 55 patients. Karyotypic changes in two separate tumors were identified in six patients; four of them had different anomalies, whereas two had cytogenetically indistinguishable alterations in the two tumors. In a patient who had two leiomyomas with karyotypically identical del(7q), the clonal tumor origin was assessed by a combination of RFLP and X-chromosome inactivation analysis. The two tumors with del(7q) had different X-chromosomes inactivated, which demonstrates that they originated independently.

The cytogenetic picture of uterine leiomyoma has similarities to that of lipoma; both tumor types have nonrandom rearrangements of 12q13–15, aberrations of 6p and 13q, ring chromosomes, and occasionally display complex karyotypes. Leiomyomas also have cytogenetic features in common with pleomorphic adenoma of the salivary gland and with myxoid liposarcoma, both of which show rearrangements of 12q13–15. Trisomy 12 is found not only in leiomyoma, but also in benign ovarian tumors. Few karyotypic similarities were noted between leiomyoma and the malignant muscle tumors—leiomyosarcoma and rhabdomyosarcoma—which might indicate separate genetic pathways for benign and malignant muscle tumors.

November 1991

Natural history, palliative treatment and prognostic factors in prostatic cancer—A population-based study from Örebro, Sweden

J.-E. JOHANSSON

From the Department of Urology, Örebro Medical Centre, S-701 85 Örebro, Sweden

The aims of this study were to investigate the natural course, progression, disease-specific survival and overall survival in patients with untreated, localised prostatic cancer; and to investigate, by means of two randomized trials, the safety and efficacy of different palliative treatments in advanced disease. All studies were population-based and prognostic factors were evaluated in both the localised and advanced stages.

Patients (223) with localised disease who received no initial treatment had a high (86.8%) 10-year corrected survival rate. Fifty-eight of them who met our current indications for radical prostatectomy had similar (87.9%) survival rates. The risk of a progressive and eventually fatal prostatic cancer decreased after five years of observation unlike the risk of dying of other causes, which exceeded by far the mortality due to prostatic cancer. Only a few patients experienced more substantial symptoms because of local tumor greowth and these were in general successfully treated hormonally. There seems to be a group of patients having 'latent' cancer with some local tumor growth but no metastatic potential. There is little room for therapeutic improvement with radical treatment (surgery or irradiation) at the time of diagnosis and such treatment should be evaluated in randomized trials with an untreated control group.

In advanced stages, estrogen treatment (74 patients) resulted in a significantly ($p = 0.05$) longer progression-free survival than did orchiectomy (76 patients). However, because of a higher rate of cardiovascular complications estrogen cannot be recommended in the combined oral and parenteral form used in this study.

In therapy-resistant cases the response was better with medroxyprogesterone acetate (51 patients) than with estramustine (51

patients). The prognosis was poor, however, the mortality rate being 70% during the first year.

The only significant prognostic factor for disease-specific survival in localised disease was tumor grade. In advanced disease, M category, T category, sedimentation rate and age were all realated to both progression and to disease-specific death. Among 300 consecutive cases in all stages, the prognostic factors of significance for disease-specific survival were M category, T category, grade, performance status, sedimentation rate and hemoglobin. The relationship of the sedimentation rate and prognosis was non-linear. The risk was lowest with a sedimentation rate of 40–50 mm/h and higher for both lower (<10 mm/h) and higher values (>63 mm/h). Sedimentation rate may be a marker in patients with a weak host defence or in those with proliferative disease.

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Lipoxygenase inhibition—effects in glioma cells in vitro

I. GÁTI

From the Department of Neurology, University Hospital, S-751 85 Uppsala, Sweden

The aim of this study was to investigate how inhibitors of the arachidonic acid cascade enzymes affect tumor growth in vitro.

We have found that specific lipoxygenase inhibitors had very potent inhibitory effects on the multicellular spheroid volume growth and on the ^{3}H-thymidine incorporation of cells cultured either as monolayers or as spheroids. The effect on the DNA synthesis was more pronounced in spheroids than in monolayers. This observation points to the significance of the lipoxygenase metabolites of the arachidonic acid cascade in the multicellular spheroids, an in vitro system which mimics the in vivo conditions of malignant brain tumors with regard to growth in a three-dimensional matrix and to the development of a central necrosis. We were able to increase the inhibitory effects of the lipoxygenase inhibitors on monolayer cultured cells by using Ca^{2+}-ionophore or membrane perturbations. This indicates a possible role of a 'stress' situation which is present in the spheroids when necrosis develops, but which is not present in the monolayers unless induced by external disturbances.

Platelet activating factor (PAF) antagonists also had antitumoral effects, primarily with regard to spheroid volume growth. Some of these antagonists with etherlipid structure had very potent antiproliferative effects on monolayers as well as spheroids. This effect was probably not related to interaction with PAF-receptors. The multicellular spheroid model offers a possibility to use the ^{11}C-labelled methionine for repeatable non-destructive testing of drug effects in vitro in analogy with positron emission tomography (PET). The lipoxygenase inhibitors, although strongly antiproliferative, had no effect on the ^{11}C-methionine uptake of the spheroids. This emphasizes the importance of understanding the functional effects of a certain drug prior to the use of PET for monitoring treatment effects. The in vitro PET-analog system can furthermore be used for drug screening.

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Cancer risks in humans after iodine-131 exposure

P. F. L. HALL

From the Dept. of General Oncology, Radiumhemmet, Karolinska Hospital, S-10401 Stockholm, Sweden

The carcinogenic effect of ^{131}I was studied in patients exposed for diagnostic purposes or as treatment for hyperthyroidism and thyroid cancer.

Cancer incidence and mortality in 10 552 hyperthyroid patients receiving a mean activity of 506 MBq form ^{131}I and followed for 15 years did not differ from what was expected, except for stomach cancer. The stomach had been exposed to a mean dose of 0.25 Gy from ^{131}I and this dose was concluded to have contributed to an increased risk. No significantly increased risk of leukemia or breast cancer was noted.

A record-linkage study of 2 968 thyroid cancer patients revealed 283 second primary tumors after a mean follow-up of 12 years. Significantly elevated risks were seen for cancer of the kidney, nervous system, and endocrine glands other than thyroid. The risk was highest 2–9 years after exposure indicating that common etiological factors or increased medical surveillance rather than thyroid cancer treatment were responsible for the increase.

The incidence of cancer and leukemia was studied in thyroid cancer patients treated with ^{131}I ($n = 834$) and by other means ($n = 1\,121$). A significantly increased overall cancer risk was seen in the ^{131}I exposed group, mainly in women, in contrast to the non-exposed patients. No significantly increased risk was seen for bladder or stomach cancer despite mean organ doses of 2.1 Gy. Since the risk increased with increasing administered activity in those receiving thyroid ablation with ^{131}I, and an elevated risk was seen in organs that concentrate ^{131}I, a carcinogenic effect of ^{131}I could not be ruled out.

The individual absorbed dose to the bone marrow was calculated for 46 988 patients exposed to ^{131}I for diagnostic reasons (77%), treatment for hyperthyroidism (21%) and thyroid cancer (2%). Mean dose to the bone marrow was 14 mGy (0.01–2 226 mGy) and the mean follow-up was 21 years. In all, 195 leukemias were found more than 2 years after exposure giving an overall standardized incidence ratio of 1.09 (95% confidence interval 0.94–1.25). It was considered to be less likely that ^{131}I influenced leukemia risk since no increased risk was seen in those <40 years of age at exposure, or 2–9 years after exposure. A similar risk of chronic lymphatic leukemia (CLL) and non-CLL also argued against a radiation effect since CLL is rarely induced by ionizing radiation.

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Metoclopramide—a representative of a new class of drugs for potentiation of cytotoxicity

S. LYBAK

From the Department of Oto-Rhino-Laryngology, University Hospital of Lund, S-221 85 Lund, Sweden

The focus of the present studies has been the evaluation of metoclopramide MCA as a sensitizer of irradiation and cisplatin treatment.

It was found that MCA sensitized irradiation of two human squamous cell carcinomas xenografted to nude mice. Using the nude mouse model, the sensitizing property of MCA on cisplatin treatment was evaluated: 1) The optimal time of MCA administration relative to cisplatin administration was found to be 8 h after cisplatin administration, 2) the sensitizing effect of MCA was not dependent on the cisplating dose, 3) MCA did not potentiate normal tissue side-effects of cisplatin treatment, in terms of weight loss and mortality, and 4) no potentiating effect of MCA could be shown on the anti-tumor effect of carboplatin.

In mice the optimal time of MCA administration to obtain the maximum sensitizing effect of ionizing irradiation was found to be 1 h before the irradiation. Using acute skin reactions after irradiation of the mice feet, and $LD_{50/30}$ after whole body irradiation as endpoints, MCA was not found to sensitize normal tissue to irradiation.

Using human mononuclear leukocytes treated in vitro, MCA was found to cause DNA damage in a dose-dependent manner, and by a mechanism independent of temperature. The DNA damage due to MCA was shown to be additive to that induced by irradiation. MCA was also found to inhibit the repair of bulky DNA lesions induced by the carcinogen NA-AAF. The inhibition of DNA repair was not due to a direct inhibition of the DNA repair enzyme poly-ADPRT.

Furthermore, the DNA damaging effect of MCA was not found to be mediated via an oxygen radical mechanism, nor was it mediated via Ca^{++} homeostasis imbalance.

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The swollen arm—a study of patients treated for breast cancer

K. SEGERSTRÖM

From the Department of Clinical Physiology, University of Umeå, S-901 87 Umeå, Sweden

Relative loss of function and development of brachial oedema are well-known complications of treatment of breast cancer and many theories have been published about their nature, cause, and incidence.

In five separate investigations, the aetiology, incidence, prognosis, pathophysiology, and treatment were studied. In all the studies, brachial oedema was defined as a difference in volume of more than 150 ml between the patient's two arms. The volumetric measurements were made by the water displacement method.

Brachial oedema occurred in 21% of patients treated with surgery alone, but in 60% of the patients who had also received high-dose irradiation to the axilla. Stiffness of the shoulder was more common among patients treated with high-dose irradiation of the axilla, which might contribute to the higher incidence of arm oedema.

Six factors were investigated that may increase the likelihood that an arm will swell after treatment of breast cancer. The highest incidence of brachial oedema was found among patients with a history of infections in the arm (89%), and in patients who has been treated with postoperative high-dose irradiation to the axilla (60%). Overweight, oblique surgical incision, infection in the arm, and radiotherapy to the axilla all correlated with arm swelling. The patient's age and whether the operation had been performed on the dominant or non-dominant side correlated less well with the incidence of brachial oedema.

Both careful volumetric measurements of the brachial oedema and relatively rough estimates of stiffness of the shoulder joint, provide acceptable indications of disability as assessed by the patient. Exceptions are common, however, and prognostic statements about arm and hand function after treatment of breast cancer should not be made as a result of a single examination. Range of shoulder movement, brachial oedema, pain, and subjective disability, may improve or worsen several years after treatment.

In a study on the arterial and venous circulation of the arms of women with brachial oedema after treatment of breast cancer, larger venous volumes were found in the oedematous arms. Venous outflow and arterial inflow at rest did not differ between the arms. Arterial inflow during the first minute of reactive hyperaemia was significantly lower in the oedematous arms than in the arms of healthy controls.

Twenty women with brachial oedema and restricted shoulder movements after treatment of breast cancer were operated on by a standard technique, with decompression of the axillary vein and division of the irradiated portion of pectoralis major. Arm volume decreased significantly in 14 patients and improvement of shoulder movement in 19 patients.

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Quality of life during cancer chemotherapy treatment—an analysis of experience of cancer patients

B. GUNNARS

From the Department of Oncology, University Hospital, S-221 85 Lund, Sweden

The primary aim of the study was to ascertain to what extent cytostatic treatment fulfills its function in terms of palliation, without the patient's overall life quality being deteriorated due to the side-effects of the treatment.

The series comprised 54 patients (breast, ovarian, lung and testicular carcinomas) undergoing cyclic treatment with cytostatics (six regimens with different toxicity).

The patients were interviewed both before the start of the treatment cycle (at hospital) and a week after treatment (at the patient's home). Follow-up consisted in the patient answering a questionnaire (67 items, written component) and a subsequent interview (oral component) at each treatment cycle during the first four months of treatment ($\leqslant 7$ cycles).

Of the somatic and mental or psychological symptoms, the highest ratings were given to alopecia where the patients distinguished between distress due to alopecia and distress at the prospect of alopecia. Tiredness, reduced muscle tone, increased need of sleep, depression, anxiety, apathy, weight loss and loss of appetite were next in rating order. Largely the same items were obtained from patients on the high and low toxic regimens respectively, though the ranking differed somewhat. However, the rating values were higher (worse) for the patients with high-toxic regimens.

While either the successive distancing of friends or their excessive concern, had a detrimental effect upon the patients, the family constituted their most important source of support.

Confidence in the treatment was on questionnaire answers rated as great; similarly, the treatment was rated as largely 'worth its price'. At interviews, however, the patients' verbal comments on these items were somewhat more cautious, although their confidence in medical science was nevertheless great—even in cases of switches in treatment failure.

The patient often has blind faith that the treatment prescribed by the physician will have a beneficial effect. Regardless of whether the treatment was accompanied by side-effects, or was even ineffective, confidence in treatment remained high among the present patients. Thus the physician has a great responsibility not to offer the cancer patient palliative treatment known to be highly toxic on any but the strongest grounds. As an aid in the choice of the optimal way of taking care of patients more studies of quality of life should be carried out in conjunction with evaluation of different regimens.

The importance of supportive resources during cytostatic treatment was emphasised by patients, even though no such items were included in the questionnaire. Thus, as access to a satisfactory support system is so essential a determinant of the patient's ability to cope, it is important that care personnel be alert to the possible lack or deficiency of such a support network.

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