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HYPERTHERMIA AS AN ADJUVANT TO RADIOTHERAPY OF MALIGNANT MELANOMA

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The possibilities of enhancing the effect of radiotherapy by adjuvant hyperthermia was investigated in recurrent or metastatic malignant melanoma. 115 cutaneous or lymphnode metastasis in 36 patients were treated with 3 fractions of irradiation alone or irradiation followed by hyperthermia either immediately (simultaneous treatment) or after an interval of 3-4 hours (sequential treatment). The radiation dose range varied between 5-10 Gy per fraction allowing a dose-response analysis. The isoeffective dose for 50% complete response after radiation alone was 26.3 Gy. Addition of hyperthermia stastistically significant reduced the dose with a thermal enhancement factor (TER) of 1.43 for simultaneous treatment and 1.24 for sequential therapy. Similar, the persistant local control was significantly improved by hyperthermia. However the simultaneous treatment enhanced also the acute skin response to the same extend as the tumor (TER 1.42), thus no therapeutic gain was obtained with this treatment. In contrast was no normal tissue enhancenment found after sequential treatment (TER 1.02 for severe erythema) therefore such treatment resulted in a significant therapeutic effect. The effect was especially prominient in larger tumors if they could be sufficiently heated, and a volume corected analysis showed a TER of 1.51.

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HODGKIN'S DISEASE AND AGE.

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Older age has frequently been associated with poor survival in studies of prognostic factors in Hodgkin's disease (HD). In the present study the prognostic significance of age was examined by multivariate analysis in relation to other known prognostic factors, most notably the patient's total tumour burden estimated as a combination of 3 variables: peripheral + intrathoracic nodal tumour burden, intraabdominal nodal tumour burden, and number of involved extranodal sites. The material consisted of a large, unselected population of 506 patients with HD treated at a single institution during 1969-83. With regard to disease free survival the only independent prognostic factors turned out to be treatment modality and total tumour burden. Age, sex, stage, B-symptoms, histologic subtype, ESR, and lymphocytopenia had no independent significance. With regard to death from HD the only independent factors were age and total tumour burden. The importance of age for mortality from HD seemed to derive at least partly from the fact that older patients had less often received adequate treatment for relapse. In patients receiving adequate treatment for relapse, age proved to have no influence on mortality from HD after relapse.
In conclusion, the results of the present study indicate that provided adequate treatment is given the chances of cure from HD would seem to be largely the same for patients with equal tumour burden irrespective of age.

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INTERACTION OF 5-FLUOROURACIL AND TOTAL BODY IRRADIATION IN MURINE HEMATOPOIETIC TISSUE

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The survival (SF) of hematopoietic stem cells (CFU-s) was studied by means of the spleen colony assay. 5-FU was given intraperitoneally in the dose range 50-500 mg/kg body weight and SF decreased and reached a minimum after 1-2 days. This was followed by a regeneration phase with a doubling time (TD) of about 28 hr, with a return to pretreatment values on day 7, and with an overshoot of SF on day 10-28. Except for no evidence of an overshoot of SF, a similar regeneration was observed after 0.75 Gy total body irradiation alone (TBI). The mean TD seemed longer the lower the dose of either 5-FU or TBI. 5-FU given 15 min before TBI resulted in a pronounced reduction in SF due to a steeper dose-response curve. After combined 5-FU and TBI, the SF rapidly decreased to a minimum at day 1, and it showed only a slight increase within the next 7 days. After this delay, the stem cells regenerated with a TD of about 30 hr, reaching pretreatment values on day 15. The delayed stem cell regeneration was not seen after 5-FU or TBI alone given in a dose which resulted in the same nadir of SF. Thus, 5-FU greatly enhances the hematopoietic damage after TBI by reducing the number of surviving stem cells and delaying the stem cell regeneration.

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LOSS OF TUMORIGENICITY OF A HUMAN BREAST CARCINOMA CELL LINE ESTABLISHED AND PROPAGATED IN SERUM-FREE MEDIUM.

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Human breast carcinoma cells from primary tumors are difficult to cultivate in vitro. Although media have been described for long term cultivation of normal human breast epithelium, proliferation of carcinoma cells is rarely obtained in these media. We have established a cell line, HMT-3909, from a ductal breast carcinoma. The cells have been explanted and propagated on collagen-coated plastic in a chemically defined medium with insulin, transferrin, epidermal growth factor, hydrocortisone, estradiol, triiodothyronine, cAMP, ethanolamine, phosphoethanolamine, fibronectin, fetuin, ascorbic acid, and trace elements. The cells in monolayer culture are epithelial as based on the demonstration of the human milk fat globule membrane antigen and cytokeratins. The HMT-3909 is aneuploid, tumorigenic in nude mice, invasive in the embryo chick heart in vitro test. However, after passage no. 18 the cells lost tumorigenicity without any gross morphological changes. Studies revealing other biological or biochemical changes in the cells simultaneous to the loss of tumorigenicity are in progress.