TRa 04

THE GERMAN THOROTRAST STUDY

G. van Kaick

The German Thorotrast Study comprises more than 5.000 persons intravascularly injected with Thorotrast and a similar number of control patients. A total of 2.334 Thorotrast and 1.912 control patients have died, with causes of death established by medical records. The number of death in the Thorotrast versus control series are as follows: Liver cancer 347/2; liver cirrhosis 292/42; myeloid leukemia 35/3; chronic lymphatic leukemia 3/2; bone marrow failure 20/1; bone sarcoma 4/1; plasmocytoma 4/1; lung cancer 46/40; pancreatic carcinoma 20/4; renal carcinoma 4/2. A clear dose effect relationship is present for liver cancer and cirrhosis. However, an influence of the bone marrow dose rate to leukemia incidence cannot yet be established. It is one of the most exciting results of the study that there is no excess rate of bronchogenic carcinomas though the lung is exposed to chronic alpha-radiation by the exhaled daughter product Thoron.

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TRa 05

Assessment of the Total Risk
of Radiation Induced Tumors at Low Doses

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Risk assessments for radiation induced tumors must be based on the extrapolation of human data to low doses and on the comparison of such data with animal studies. A survey will be given of the potential and of the limitations of these two methods.

The determination of dose dependences for radiation induced neoplasms necessitates in all cases the estimation of the temporal variation of tumor rates throughout the life time of the exposed individuals. Because of the multiplicity of parameters the analysis must largely rely on mathematical models. Essential aspects of such models, such as the widely used proportional hazards model, will be illustrated with reference to epidemiological and experimental studies.

With the revision of the dosimetry for the survivors of the atomic bomb explosions one has lost the apparent source of information on the induction of neoplasms in man by neutrons. Human data for densely ionizing radiations exist now only for α-rays, and such data can not readily be extrapolated to other types of densely ionizing radiations. Considerations on the revision of quality factors in radiation protection must therefore be based on animal studies and on transformation experiments with cell cultures. The synopsis of existing data has led to the proposal that the ratio of quality factors for densely ionizing and sparsely ionizing radiations be substantially increased above current values.

RTh 01

QUALITY ASSURANCE IN COOPERATIVE THERAPY STUDIES
(UNDER RADIOTHERAPEUTICAL ASPECTS)

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In cooperative studies, the criteria for selecting patients, the therapeutic regimens and the methods of evaluating are to be defined exactly. Quality assurance programs are an attempt to minimize the protocol deviations and to quantitate the extend of variance. In multimodality studies, a quality assurance program for each modality is required.
As an example of quality assurance in radiotherapy, the experiences of the Ewing's sarcoma study "CESS 81" of the German Society for Pediatric Oncology are reported. Following the cancer and Leukemia Group B (CALGB), the quality of radiotherapy can be quantitated in form of a "performance score": the product of the compliance rate and the appropriateness for every participating institution.
Quality assurance programs are essential requirements for comparing the results of institutions in a cooperative group. They control the validity of combined institutional studies, improve the "performance" of the participating institutions and increase the reliability of the collected data.
Quality assurance programs are time consuming, expensive, but basically to reliable statistical analysis of such cooperative studies. A higher scientific quality of these studies can be achieved, if therapeutical results are correlated with the protocol compliance or a "performance score", respectively.

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RTh 02

CISPLATIN, A SENSITIZER OF HYPOXIC MAMMALIAN CELLS?

W. Ziegler

The effect of simultaneous treatment with Cisplatin and gamma irradiation upon the survival of hypoxic mamalian cells was studied. The four cell lines used were Chinese hamster fibroblasts (B 14), Syrian hamster kidney cells (HaK), HeLa cells and human melanoma cells (MM). While under aerobic conditions the presence of Cisplatin had no influence upon the shape of the radiation dose-response curve of B 14 and HeLa cells, in HaK and MM cells an increased curvature indicated a radiosensitizing effect of Cisplatin. Under hypoxic conditions, Cisplatin did not alter the shape of the radiation survival curve of B 14, HaK and MM cells. In HeLa cells, however, the difference between the curves obtained with radiation only or in the presence of Cisplatin indicates radiosensitization of hypoxic cells down to the survival level of 0.01, the dose modifying factor roughly equalling 1.2. Combined with irradiation, Cisplatin can act as a specific sensitizer of aerobic cells (e.g. HaK and MM cells) or hypoxic cells (e.g. HeLa cells). The drug may also lead to radiosensitization both under aerobic and hypoxic conditions as in H 4 cells (Int.J.Radiat. Oncol.Biol.Phys. 7, 929, 1981) or not influence radiosensitivity at all (e.g. B 14 cells). Thus, Cisplatin does not unequivocally act as a hypoxic cell sensitizer in eucaryotic cells. Under the same experimental conditions, Misonidazol showed a marked radiosensitization in all four cell lines, which was specific to hypoxic cells.

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