WEDNESDAY 1 NOVEMBER 1995

Teaching lectures

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HIGH-DOSE—LOW-DOSE

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For certain malignancies the curative effects of chemotherapy are worse if the patient received less than the optimal chemotherapy dose. Much less is known concerning the value of high-dose chemotherapy for solid tumours. With the help of stem cell reinfusion and haematopoietic growth factors it is possible to get up to a 10-fold dose increase for certain chemotherapeutic drugs.

High-dose chemotherapy may be interesting for a number of solid tumours such as non-seminomatous testicular carcinoma, breast carcinoma in the metastatic and adjuvant setting, ovarian carcinoma, tumours of young adults such as Ewing sarcoma and small cell lung carcinoma. For most of these tumour types and settings it will be necessary to perform randomized studies before firm conclusions can be drawn. This is for example especially important for patients with breast carcinoma with >3 positive axillary lymph nodes. Preliminary data from various groups show compared to historical controls treated with standard adjuvant chemotherapy, favourable results of adjuvant chemotherapy containing high dose chemotherapy. The potentially currently safer therapy of high-dose chemotherapy may reveal in the near future the role of high-dose chemotherapy in solid tumours.

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MODERN TUMOUR PATHOLOGY: DIAGNOSTIC AND PROGNOSTIC IMPLICATIONS OF IMMUNOCYTOCHEMICAL AND MOLECULAR DATA

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Modern tumour pathology has to cope with two major challenges: (i) to provide more precise diagnoses, and (ii) to be able to recruit from tumour tissue samples all the parameters useful to predict the expected biological behaviour of individual tumours and their more likely response to different therapeutic approaches. In the effort to achieve these goals, pathologists have taken the greatest advantage from the application of novel procedures (namely immunocytochemistry and molecular biology techniques) coupled with classic morphological features of the neoplastic cells. Studies on the expression of structural or functional cell markers and on genetic abnormalities of oncogenes and tumour suppressor genes have already proven to be of invaluable effectiveness in the assessment of the histogenesis and biological behaviour of human malignancies, and in predicting the clinical outcome of the affected patients as well.

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MOLECULAR DIAGNOSIS OF EWING'S TUMOURS

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The Ewing family of tumours is characterized by specific fusion transcripts which link the EWS gene with either of the FLI-1, ERG or ETV1 members of the ETS family of transcription factors as a result of chromosome rearrangements. Analysis of a large series of tumours was performed. No correlation between the type of fusion transcript and localization, phenotype or extension of the tumour was observed. Based on the sensitivity and specificity of the detection of these alterations by the Reverse Transcriptase PCR technique, the presence of small number of Ewing cells was investigated in blood, bone marrow and stem cell harvests from patients with Ewing's tumour. This method enables the detection of less than one tumour cell per million of normal cells. At diagnosis, tumour cells could be detected in one third of samples analysed. The relevance of these molecular markers in the clinical assessment of Ewing's tumours will be presented.

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NEW TRENDS IN BRACHYTHERAPY

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As we look towards the future of brachytherapy, there are many new trends that may help to improve cancer treatment. The following areas will be addressed:

1. The use of current and new imaging devices before and during brachytherapy to better define and select the tumour, target, and implanted treatment volumes.
2. The development of three-dimensional target planning systems to provide superior dosimetry and dose volume histograms which will result in optimal treatment planning for either brachytherapy alone or with external beam irradiation.
3. Use of remote afterloading systems with either low dose rate (LDR), intermediate dose rate (IDR), pulsed dose rate (PDR), and/or high dose rate (HDR) incorporated into the more accurately defined tumour and target volumes.
4. The development and application of better mathematical models to correlate LDR, IDR, PDR, and HDR.
5. Technical improvements such as the development and use of new miniature radionuclides, permanent interstitial implants with the use of biologically inert materials, and highly sophisticated remote afterloading systems.
6. Potential applications of combining fractionated HDR with continuous LDR irradiation.
7. Combining brachytherapy with: (a) chemotherapeutic agents; (b) hyperthermia: (c) external beam irradiation.
8. Intraoperative brachytherapy.

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CYTOKINES IN METASTATIC RENAL CELL CARCINOMA

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Interferon alpha as well as Interleukin 2 were extensively used during the past decade specially in the treatment of metastatic renal cell carcinoma (MRCC). Interferon alpha (IFN) gave response rates from 5 to 15% and Interleukin 2 (IL2) was reported to give 8 to 35% response rate including 5 to 10% of complete persistent remissions. Our past experience using either IV IL2 alone or together with IFN or this combination subcutaneously gave response rates from 15 to 25% and these results do not seem different according to the treatment modalities. In 1991, together with our French colleagues, we designed a randomized trial in MCRR. Patients could receive continuous infusion of IL2, or IFN or combination of both cytokines. Different clinical prognosis factors as well as putative prognosis biologic parameters were taken into account response rates and survival are the major end-points of this study. 470 patients were registered in 4 years and inclusion will stop by 30 June 1995. The data we expected from this trial could give us bases to select patients who may benefit of this treatment. In addition, new approaches in the treatment of MCRR must be set up.