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Testicular cancer – Staging, treatment and outcome

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Germ cell cancers of the testis, the commonest malignancy of young males, are rapidly increasing in incidence; cure is possible in, overall, 95% of cases. The major challenge is to cure all patients with metastatic disease with chemotherapy ± surgery. The International Germ Cell Consensus Classification has recently been introduced in order to allocate patients to good, intermediate and poor prognosis groups on the basis of height of serum markers (AFP, HCG, LDH), presence of non-pulmonary visceral disease and presence of mediastinal primary site (non seminoma only). Current trials in metastatic disease seek to maintain cure rates whilst minimising toxicity (good prognosis, cure rates >90%) or to improve survival with novel treatment approaches (intermediate, poor prognosis, cure rates c. 70%).

Stage I disease is common. Fresh treatment approaches seek to minimise use of irradiation (seminoma), chemotherapy (non seminoma) and CT scans.

Epidemiologists continue to explore underlying events (falling sperm counts, increasing incidence of maldescent), however germ cell cancers will remain a significant challenge for the foreseeable future.

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Malignant tumors in patients with HIV infection

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It is estimated that malignant tumors, in particular Kaposi's sarcoma (KS) and non-Hodgkin's lymphoma (NHL) complicate the course of over 40% of patients with HIV infection. Moreover, because of the longer survival of patients with HIV infection due to advances in antiretroviral therapy and prophylaxis and treatment of non neoplastic opportunistic complications of HIV infection, there will probably be an increase of cancer in HIV setting. KS, high and intermediate grade systemic NHL, primary NHL of the central nervous system and invasive cervical cancer are considered diseases indicative of AIDS in patients with HIV infection. There is also an increase of non invasive intraepithelial lesions of the ano-genital squamous epitelium that may be precursors to invasive cancer both in men and women with HIV infection. The natural history of cancers in patients with HIV infection differs from that of the general population. Unusual aspects of tumor localization, growth behaviour and therapeutical response, distinguish tumors in patients with from those without HIV infection. The pathologic and virological aspects of HIV-related tumors are peculiar and for example a pathological classification of HIV associated systemic NHL has been formulated. The treatment of HIV-related neoplasms is controversial as it is not clear whether conventional therapy and in particular chemotherapy may be safely administered and it is able to modify the natural history of these malignancies.

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An introduction to gene therapy

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The number of gene therapy trials (mostly Phase I) exceeds 200. In the beginning of 1997, more than 2100 patients have been enrolled. Starting in 1990 with the pioneering gene therapy treatment of some children suffering from a genetic disease, adenosine deaminase deficiency, the field has more and more moved to cancer gene therapy. Several strategies with therapeutic purposes are being followed. 1. Reversal of the tumor cell phenotype/selective induction of apoptosis by transfer of functional tumor suppressor genes or oncogene-antisense molecules which can result in cell growth arrest and apoptosis. 2. 'Suicide gene' strategy: Certain gene products like the HSV thymidinkinase (TK) can convert nontoxic products into toxic compounds, thus TK expressing tumor cells kill themselves. 'In vivo' TK gene transfer into tumor cells and subsequent prodrug application can result in tumor cell death. 3. Engineering tumor vaccines: Expression of genes encoding immunostimulatory molecules (cytokines, T cell costimulatory molecule B7) in tumor cells can increase their immunogenicity. Such cells can be rejected by the involvement of T cells recognizing tumor-associated or -specific antigens, eventually resulting in systemic tumor immunity. Animal models with engineered tumor cells as vaccine come to the conclusion that this approach is promising provided it is being done in a situation of 'minimal residual disease'. Critical issues applying to one or several of the approaches are: convenient and efficient 'in vivo' gene transfer systems, stable vs. transient gene expression, immunogenicity of the gene transfer system, safety, patient selection, reliable early endpoint parameter to measure therapeutic efficacy.

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Controversies in brachytherapy for localised prostate cancer

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Brachytherapy for early prostate cancer was discredited in the 1980's because the technique of manual seed placement into the surgically exposed prostate could not reliably irradiate the gland and both morbidity and recurrence occurred as a result of hot spots and cold spots. Where satisfactory implants were achieved, however, results were shown to be good. New techniques of percutaneous transrectal ultrasound guided source placement now make it possible to achieve satisfactory source distribution in the vast majority of patients. It is now possible to treat with permanent radioactive seed implants or temporary removable implants at both low, medium and high dose rates. The questions and controversies which remain include which patients to treat and by what technique, what dose is required to sterilise local disease, what is the contribution of external beam radiation to the pelvis. There also remains some controversy about the most relevant end-points for evaluation after treatment. These include PSA relapse free survival with a PSA level as yet undefined; post treatment biopsy and the role of repeat staging investigations.