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CHEMOTHERAPY (CT) WITH CISPLATINUM (P), METHOTREXATE (A), MITOMYCIN C (M) AND BLEOMYCIN (B) [PAMB] IN UNRESECTABLE OR METASTATIC PENILE CARCINOMA (PC).
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The role and place of CT in PC is basically unknown.

We have designed a pilot study to evaluate the anti tumour effect of CT.

From February 1984 to February 1993, 19 patients (pts) with advanced PC were treated with CT with the same regimen we treat our head and neck cancer pts.

Pts received A 30mg/m2 IV on day 1, P 20mg/m2 and B 5mg/m2 both IV, days 1 to 5, and M 10mg/m2 IV day 5, every 28 days.

Median age was 46 years (24-75), median performance staus (WHO) 2 (0-3). Fourteen pts had clinical stage (UICC) and 5 stage IV.

Two pts are too early to evaluate. Four pts were lost to follow-up during first cycle of treatment and were considered as early deaths and included in disease progression (DP) category of response.

After a median of 3 cycles (1-7) we observed 3 (17.6%) complete responses (CR), 7 (41.2%) partial responses (PR), 3 (17.6%) no change (NC) and DP in 4 (23.5%) pts.

Median time to response is 2 (1-4)m, median duration is 3+ (2+ - 16+)m. Survival data has been hampered by loss of follow up of most pts which is a common feature in our Institution.

Toxicity during treatment follows: nausea and vomiting grade (G) II in 31.6%, III in 15.8%; alopecia G III in 63.2%; leucopenia G III in 10.5%, G I or II in 31.5%; G I increase in serum creatinine in 10.5%; and fever in 21.0%.

We conclude that in spite of its toxicity this regimen is effective in producing objective responses and may contribute to lessen treatment morbidity if used earlier in the natural history of this disease.

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PILOT STUDY OF REAFERON R-IFN-2A (R), ADRIAMYCIN (ADR) AND WHOLE - BODY HYPERTHERMIA (WBH) IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (RCC) : PRELIMINARY RESULTS.
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11 patients (pts) with multiple RCC metastases in lungs (1-2 years after nephrectomy) have been treated with R 3 million U/sq. mm, days 1-7; Adr 60 mg/sq.m iv, the 4th day, 5 pts received Adr under WBH (41.C-41.8°C, 180 min.). The courses of treatment were repeated every 4 weeks. There was no clinical and laboratory III-IV grade toxicity. Of the 6 pts treated without WBH, 1 showed PR, 3 - stabilization, and 2 had no response; 4 pats died 4,5 and 11 months after; 2 pts are alive for 6 and 12 months. Of the 5 pts treated under WBH, 1 showed CR, 1 - PR, 1 - stabilization, and 2 had no response; 2 pts died 6 and 7 months later; 3 are alive for 12, 12 and 18 months. The results indicate that WBH can enhance the antitumor effect of R and Adr on RCC metastases in lungs.

Prostate Cancer

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EXPRESSION OF TENASCIN IN THE RAT PROSTATE AFTER ANDROGEN ABLATION BY CYPROTERONE ACETATE
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Tenascin / hexabrachion protein is an extracellular matrix protein proposed to be correlated with epithelium mesenchyme interactions during development and oncogenesis. The goals of this study were to analyse if 1. tenascin is expressed in the normal prostate; 2. expression of tenascin is influenced by androgen ablation; and 3. whether analysis of immunoreactivity provides evidence for the involvement of epithelium mesenchyme interactions after androgen ablation and apoptotic cell death.
We demonstrated by use of immunohistochemistry and a semiquantitative scoring that the abundance of tenascin immunoreactivity in the stroma of the prostate contrasted with its scarity in epithelial regions. An increased expression of tenascin was detected following androgen ablation either by Cyproterone acetate or orchiectomy.
The enhanced expression of tenascin after treatment with Cyproterone acetate seems not to be related to the gestagenic potency of the compound since a progesterone treatment in a similar experiment could not stimulate tenascin expression.
In earlier studies we found that the process of differentiation is accompanied by a loss of tenascin expression whereas it appears that dedifferentiation of prostate tissue by androgen ablation is associated with an enhanced induction of tenascin expression. This indicates that the elimination of epithelial cells by androgen ablation correlates with a remodelling of the extracellular matrix and an increase of stromal tenascin expression. Our data strongly suggest that the process of apoptotic cell death during prostate involution by androgen ablation requires epithelium mesenchyme interaction.

Key words : Prostate cancer, antiandrogens, tenascin

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FAMILY AGGREGATION AND THE RISK OF PROSTATE CANCER

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Cancer of the prostate is the most common cancer among males. Several epidemiologic studies have shown multifactorial genesis of prostate cancer.

We performed a case controlled study to estimate the relative risk of developing prostate cancer for men with a positive family history. Extensive cancer pedigrees were obtained on 224 men with prostate cancer and 135 spouse controls. 31 of the 224 patients with prostate cancer (13.8%) gave a positive family history of the same cancer. In four of these families (1.8%) we have found prostate cancer in at least two family members. In 28 families (12.5%) of the prostate cancer patients the affected men have been first degree family members. Prostate cancer occured in only 5 cases (3.7%) of the 135 control group families.

This indicates about a fivefould difference in occurence of cancer of the prostate among first degree family members (father or brother) of the case group with an odds ratio (OR) of 5.6 and 95% CI, 1.8 - 17.9.

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THE DILEMMA OF POSITIVE PROSTATECTOMY MARGINS

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Histologically involved margins are often found in the specimen after radical prostatectomy undertaken for clinical stage B ($T_2N_0M_0$) disease. What, if any, treatment and when therapy should be instituted remains controversial. We analyzed retrospectively 22 patients treated definitively after radical prostatectomy from 1972 to 1983. Eleven were treated in the immediate postoperative period and 11 only after local recurrence, without demonstrable distant metastases, 2–9 years later (median 41 months).

We could not demonstrate any significant differences between the two groups. Clinical tumor control in the prostatic bed was achieved in 10 of the 11 pathological T_3 patients treated post-operatively and 11/11 original clinical T_2 patients treated after palpable local recurrence. Relapse-free survival was 2 v. 3 patients and death from prostatic cancer 5 v. 4 patients for early v. delayed irradiation. One patient is alive with hormonal control and 3 died of intercurrent disease in each group. Duration of survival was the same when measured from the date of prostatectomy.

Clinical judgment now dictates which patients are treated postoperatively. PSA values may prove useful in selecting patients for local irradiation or for systemic therapy.

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PRETREATMENT PSA IS A POWERFUL INDEPENDENT PREDICTOR OF OUTCOME FOLLOWING TREATMENT OF PROSTATE CARCINOMA BY RADICAL RADIOTHERAPY. Zietman A.L., Coen J., Shipley W.U., Efird J.T. Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA 02114, USA.

461 patients treated with radical radiation therapy at the M.G.H between 1988 and 1991 with pre-treatment and one or more post-treatment PSA values have been investigated in this study. Outcome was analyzed in an actuarial fashion using clinical disease-free survival and biochemical disease-free survival (freedom from a rising PSA) as endpoints.

The median pretreatment serum PSA value (ng/ml, Hybritech or Abbott Assay) was a function of T stage: T1a - 1.7, T1b - 5.7, T2a - 8.8, T2b - 10.4, T3 - 17.3, T4 - 58.1. 89.5% of all patients followed for greater than one year achieved a post-irradiation nadir value in the normal range (0 - 4.0). 34.7% had a nadir value in the castrate range (<0.5). For all T stages the likelihood of being disease-free at 4 years was significantly lower when PSA was used as an endpoint than when clinical evaluation alone was used (T1b [n=34] 80% vs 100%, T2a [n=58] 85% vs 100%, T2b [n=156] 32% vs 63%, T3 [n=186] 31% vs 58%, and T4 [n=14] 29% vs 69%). For the whole group at 4.5 years clinical control was 66% but biochemical control only 39% ($p<0.05$). Serum PSA is a sensitive detector of early relapse.

The likelihood of being free from rising PSA at 4 years was a direct function of the initial PSA value (PSA <4.0 89%, 4.0-9.9 69%, 10.0-19.9 64%, 20.0-49.9 12%, >49.9 6%). For T1-2 patients with initial PSA less than 20ng/ml it stood at 92% but when greater than 20 ng/ml the projected figure was zero. The corresponding 4 year freedom from biochemical relapse rates for T3-4 patients were 50% for those with an initial PSA <20 ng/ml and 10% for those with initial PSA >20ng/ml. The prognostic power of the initial PSA was independent of stage, grade, age, and prior TURP in a multivariate analysis. An initial serum PSA of >20ng/ml is therefore a powerful predictor of likely failure with conventional radiation therapy .