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HORMONAL MANIPULATION IN ADVANCED PROSTATE CARCINOMA.
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One hundred and fifty pts. with advanced prostate carcinoma were treated by hormonal manipulation. 119 pts. (79%) had metastatic disease and 31 pts. (21%) had locally advanced tumor. 25 pts.(17%) underwent bilateral orchiectomy and 125 (83%) were treated by LHRH agonists depot injections (Decapeptyl 3.75mg. or Zoladex 3.6 mg., every four weeks). Subjective improvement was achieved in 83/92 (90%) of symptomatic pts. PSA level dropped to normal in 54 pts. (64%) and to less than 50% of initial value in 27 pts. (32%). Median follow up was 16 months (2-118). The two year actuarial survival rate was 76% for all pts., 100% for those with localised disease and 74% for those with metastatic tumor ($p<0.001$). Pts with initial PSA level lower than 80 u/ml had a better survival than those with higher level (88% vs. 60%, $p<0.02$). No survival difference was observed between treatment options. Median time to relapse was 17 months (4-115).Conclusion: hormonal manipulation is efficient in the treatment of advanced prostate carcinoma. Extent of disease and initial serum PSA level correlate with survival.

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How often does serum prostatic specific antigen (PSA) increase prior to clinical progression of prostate cancer (PC)?
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The ongoing present study raises the question how often increasing PSA levels (≥ 50% elevation of baseline value) precede clinical progression (clinical examination, bone scan) in 2 groups of pts with PC: Group 1: 16 pts had loco-regionally confined PC at diagnosis and did not receive hormone manipulation initially (T1-2: 4 pts; T3: 12 pts; TX: 2 pts; NO: 1 pt; N+: 11 pts; NX: 4 pts). 5 pts were treated by ^{125}I-implantation, while 11 were observed without therapy. Median baseline PSA (before significant elevation) was 37µg/l (range: 2-170µg/l). All 16 pts progressed clinically during follow-up. In 11 pts PSA increased significantly a median of 9 months (range: 1-21) prior to clinical progression. In 5 pts PSA did not increase before progression was detected clinically. Group 2: 14 pts progressed during their primary androgen suppressive treatment which was started due to distant metastases in 8 pts and due to N+ disease or locally progressing tumours in 6. In 8 pts significant PSA elevations were observed for a median period of 5 months (range: 3-13) prior to progression. In 6 pts no PSA increase was found before the pt progressed. Conclusion: Independent from hormone manipulation, serum PSA does not increase significantly above the baseline level, in approximately one third (11 of 30) of the pts with PC prior to clinically detectable progression. This high percentage of "false negative" PSA values limits at present the use of serum PSA as an early tumour marker of progressive PC.

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EFFECTS OF OESTROGENS AND PROGESTOGENS ON THE MEMBRANE PERMEABILITY AND GROWTH OF HUMAN PROSTATIC CARCINOMA CELLS (PC-3) IN VITRO
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Oestrogens and progestogens have been used in the management of prostatic carcinoma in different stages. The effects of these compounds are related to their suppressive effect on the hypothalamic-pituitary-testicular axis, but other mechanisms have also been suggested. The present study was designed to investigate if the hormone-resistant human prostatic cancer cell line (PC-3) is sensitive to oestrogens or progestogens and to elucidate possible mechanisms of action. Both oestrogens and progestogens in high doses (10^{-5}M) suppressed tumour cell growth. At these high doses MPA most effectively reduced the uptake of ^{86}Rubidium Chloride, indicating the strongest effect on ion transport and membrane permeability. Effects was also seen after oestrogen treatment. It is suggested that oestrogens and progestogens have direct cytotoxic effects on prostatic carcinoma cells in vitro, possibly by an effect on the cell membrane.

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PHASE I-II STUDY OF THE SOMATOSTATIN ANALOGUE SOMATULIN IN HORMONE REFRACTORY PROSTATIC CANCER (HRPC)
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Somatuline (BIM 23014) was found as effective as castration in a rat prostate tumor model (R3327-H). Therapeutic benefit was also demonstrated in the hormone resistant phase of this tumor model following castration. Activity of BIM may be due to the reduction of growth factor levels such as IGF 1. The therapeutic efficacy anf safety of BIM was assessed in patients (pts) with metastatic HRPC. Thirty two pts were included in a multicenter pilot study between 91 and 93. To date, 29 pts are evaluable. The mean age was 71 years. ECOG performance status (PS) was 0 in 15 pts and > 0 in 14 pts. All pts had bone metastasis with bone pain in 16 cases. Prostate Specific Antigen (PSA) level was increased in all pts (mean : 412 ng/ml ; range : 10.3 - 5700). BIM was aduninistered intra-muscularly at a dose of 3 mg every week till disease progression. The mean number weeks of BIM therapy was 12 (2 - 32). PS and bone pain improved in 7 /14 pts (50 %) and 6 / 16 pts (37.5 %) respectively. More than 25 % PSA regression was observed in 6 pts (21 %). Four of them had significant clinical improvement and > 75 % PSA level reduction.. Response duration was 6 months +. There were no complete remissions. Toxicities were minimal : transient mild diarrhea and abdominal pain were observed in 15 pts (54 %) and 6 pts (22 %) respectively. Determination of BIM and IGF 1 plasma levels is ongoing and results will be presented. BIM administered weekly to metastatic HRPC pts was well-tolerated and demonstrated antitumor activity.

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SMALL-FIELD RADIATION THERAPY FOR CARCINOMA OF THE PROSTATE.
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One hundred consecutive patients with Stage B (78) and C (22) prostate cancer treated with external beam irradiation between 1988 and 1992 were analyzed. Median age was 73, median pretreatment PSA was 17 ng/ml (mean 36). There were 21 well, 67 moderately, 10 poorly differentiated adenocarcinomas. Treatment technique was 4-field "box" (93 patients) and split-arc rotation (7 patients). All patients were treated with an average field size of 10.8 x 10.6 cm for both AP-PA and lateral fields. Customized tertiary blocking based on CT information was used to treat the prostate with a 2 cm margin of periprostatic tissue. Dose was 66 Gy in 33 fractions for Stage B and 70 Gy in 35 fractions for Stage C patients. Median follow-up time was 24 months (12-56); 14 patients had local recurrence, 6 patients developed distant metastases, 11 patients have died. The median 6-month post-treatment PSA level was 3 ng/ml. There was no significant acute or chronic toxicity. These preliminary data suggest that the use of small fields yields control rates similar to those reported with whole pelvis irradiation.

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SUPERIOR PSA RESPONSE IN CONFORMAL XRT OF PROSTATE CANCER
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Conformal irradiation (CRT) decreases the morbidity of prostate cancer treatment, but no published data attest to the ability of CRT to control disease. Therefore, we compared PSA response at one year among similarly staged patients treated by conformal techniques to those treated with conventional approaches, looking for an early indicator of tumor response. Patients with locally advanced disease were treated by pelvic fields followed by prostate field conedowns; those with early stage/low-grade disease received only prostate field irradiation. Between 8/87-7/90 treatments used conventional polygonal beams without immobilization. Between 4/89-2/92 prostate treatments have utilized rigid immobilization and CT-based beams eye view field design. Median doses were 70 Gy (66-73 Gy) and 70.2 Gy (64.8-75 Gy) for conventionally and conformally treated patients, respectively. Daily fraction size was 1.8 Gy for conventional treatment and 2.0 Gy for conformal therapy. Baseline PSA data are available on 176 consecutive patients treated conformally and 77 consecutive patients treated conventionally. Stage distribution is comparable for both techniques. Among those receiving only prostatic field irradiation, 12-month PSA values returned to normal in 95% and 100% of conformally and conventionally treated patients, respectively. Among those receiving pelvic irradiation prior to prostatic conedown, 12-month PSA values returned to normal in 93% of conformally treated patients and 38% of conventionally treated patients ($p=.003$). As measured by PSA, conformal techniques produced responses that were significantly better than conventional techniques in locally advanced disease, while equivalent outcome was seen for early stage disease. These results, coupled with our previously documented reduction of acute and chronic sequelae, support the continuing study of CRT as a potentially more effective method of treatment prostate cancer.