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COMPARISON OF PROSTATE SPECIFIC ANTIGEN AND PROSTATIC ACID PHOSPHATASE IN THE MANAGEMENT OF PROSTATIC CANCER.

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Prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) have been evaluated in patients with prostatic cancer. All patients, who participated in a Phase III trial (n=110), had disseminated disease and received first line endocrine treatment of either orchidectomy or a monthly injection of a depot luteinising hormone-releasing hormone analogue (Zoladex). Serum samples were analysed for PSA and PAP at 0,3, 6 and 12 months and patients were clinically assessed at 6 and 12 months according to UICC criteria. At diagnosis 97% and 72% of all patients had elevated PSA and PAP concentrations (> 4ng/ml) respectively. Patients with progressive disease had significantly high PSA and PAP levels at both assessments. A small number of patients in the 'complete remission' group had both PSA and PAP levels within the normal range after 3 months of treatment. Similarly, both PSA and PAP levels steadily declined in the group of patients who had partial regression of the disease. The patients with stable disease however, had a significant rise only in their PSA levels at 12-month assessment. This data suggest that PSA is more sensitive than PAP in those patients who have a 'slow progression' of the disease.

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TRANSPLANTABLE HUMAN PROSTATIC CARCINOMA (PC-82) IN ATHYMIC NUDE MICE: A MODEL TO STUDY ANDROGEN REGULATED TUMOR GROWTH

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The hormone-dependent human tumor line, PC-82, which was established almost 10 years ago, has been maintained in nude mice for 35 subsequent mouse passages. Androgen-withdrawal from tumor-bearing intact male mice (carried out by castration or by estrogen treatment) resulted in tumor growth arrest and in a gradual decrease of the tumor volume. The take and growth of the tumor tissue in intact male mice was influenced by the great variability of circulating testosterone (T) in the plasma of these animals. T-containing Silastic implants were shown to improve the hormonal environment of the tumor in the host animal and facilitated hormonal manipulation of tumor-bearing mice as well. By the use of PC-82 bearing T-implanted female mice we investigated the effects of androgen depletion and repletion on the tissue levels of androgens and on the proliferative activity of the tissue. To monitor proliferative responses in the PC-82 tumor tissue Ki-67 monoclonal antibody, directed against a proliferation-associated nuclear antigen, was proven to be a very suitable marker. The approach of hormone-titration in PC-82 bearing mice, which is performed at present, may yield information on the minimal concentration of androgens in plasma and tumor tissue that is required to support growth of prostatic carcinoma tissue.

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THE PHARMACOLOGICAL AND ENDOCRINE ASSESSMENT OF THREE DIFFERENT ANTI-ANDROGEN REGIMENS COMBINED WITH A VERY LONG ACTING GONADROTROPIN RELEASING HORMONAL ANALOGUE

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This study evaluated the possibility of preventing the initial increase in serum testosterone levels associated with the administration of LHRH analogues. Eighteen patients with symptomatic advanced prostatic cancer were randomised to one of three treatment regimens. Six patients were treated with Cyproterone acetate 50 mg tds, six with Cyproterone acetate 100 mg tds, and six with Flutamide 250 tds for one week prior to, and for the first month of treatment with monthly depot buserelin. In each patient serum testosterone, luteinizing hormone, follicle stimulating hormone, acid phosphatase and alkaline phosphatase were measured sequentially. Castrate testosterone levels were achieved at the end of three weeks treatment. One case of tumour flare occurred with Cyproterone acetate 50 mg tds.

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COMPREHENSIVE IMMUNOHISTOCHEMICAL INVESTIGATIONS OF THE PROSTATE AND PROSTATE CARCINOMAS.

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The immature epithelium of the prepuberal prostate is positive for PAP, PSA, keratins from stratum corneum, the keratins 7, 8, 18,and 19, vimentin, and binding sites for the peanut agglutinin (PNA). After puberty, the markers PAP, PSA, CEA,ACT, the keratins 8 and 18 and focally vimentin are restricted to the secretory epithelium, keratins from stratum corneum to the basal cells. The other markers and focally the blood group antigens (ABO) occur in both cell types. Common and papillary prostate carcinomas immunohistochemically behave exactly like the secretory epithelium from which they obviously arise. In contrast, primary squamous cell carcinomas share most of the immunohistochemical features with the basal cells which can be regarded as their stem cells. The estrogen receptor (ER) is demonstrable by a modified ER-ICA-test in the nuclei of the stromal fibrocytes and partly of the smooth muscle cells and of the hyperplastic basal cells. Analogous findings are obtained with the receptor-associated protein ER-D5 which is expressed intracytoplasmatically. 5 carcinomas are ER-negative. 15 of 100 tumors are mostly focally positive for ER-D5. In nodular hyperplasia, estrogens could induce a proliferation of the ER-positive stroma. Obviously they do not act directly on carcinoma but via the hypophyseal-testicular axis.