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TESTOSTERON SERUM LEVELS IN THE INITIAL PHASE TREATMENT WITH LH-RH-ANALOGA IN COMBINATION WITH ANTIANDROGENS IN PATIENT WITH METASTATIC CARCINOMA OF THE PROSTATE

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The present paper describes randomized investigations on the influence of two antiandrogens with different mechanisms of action (flutamide, cyproterone acetate) alone and in combination with the LH-RH agonist buserelin on serum LH and testosterone concentration.
Testosterone rose rapidly in all patients in the groups which were treated with buserelin alone or with the combination buserelin plus flutamide and reached a maximum level after three to six days and fell to below the castration level after two to three weeks.
In group III (after pretreatment with cyproterone acetate over 28 days), the LH and testosterone values fell markedly compared with the initial values, but rose again after addition of buserelin, though not in excess of the initial value, and were in the castration range after three weeks.
The investigations have shown that pretreatment with CPA prevents the rise of LH secretion and the fall of testosterone below the initial values owing to the subsequent buserelin treatment, in contrast to treatment with buserelin plus flutamide. The flare-up can thus also be avoided by pretreatment with CPA.

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NODULAR PITUITARY HYPERPLASIA AFTER LONG TERM TREATMENT WITH GOSERELIN (ZOLADEX)

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In the presented case we studied morphologically detectable changes in the pituitary gland by immunohistochemistry for the first time in a patient,who was treated for 16 months with 3.6 mg Goserelin subcutaneously every 28 days due to advanced prostatic cancer.As Goserelin suppresses FSH and LH by down regulation of pituitary receptors with subsequent inhibition of testicular testosterone production this treatment is equivalent to orchidectomy.
At autopsy we found a partially diffuse and nodular hyperplasia of growth-hormone (GH) and adrenocorticotropin (ACTH) producing cells resulting from long term treatment with Goserelin. Hyperplasia of the ACTH producing cells may be interpreted as a secondary hyperplasia due to vicarious additional production of androgens in the adrenal cortex. Such an additional production of androgens may consecutively cause deterioration of the clinical course of disease.
Bearing in mind that remissions in hormonally escaped prostatic cancers can be achieved by additional hormonal measures,the question arises if hormonal relapse is really caused by testosterone independence alone or by a successful partial compensation of androgen deficiency by the adrenal gland as well. In that case the concomitant administration of an antiandrogen might be beneficial in the hormonal management of prostatic cancer.

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COMPLETE RESOLUTION OF HIPPOURIS SYNDROME WITH DECAPEPTYL IN A PATIENT WITH PRESACRAL MASS AND UNKNOWN PRIMARY

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A 69 y.o who had prostatectomy 18 years ago was admitted with lumbosacral pain, inability to walk disordered rectal and bladder function and weight loss; physical examination revealed decreased strength of pelvic girdle muscle, quadriceps atrophy, decreased tendon reflexes, abolished tunning fork below knee, S2-S3 sensory loss and rectovesical dysfunction CAT scanning revealed the presence of a mass invading the sacral plexus. Bone scanning disclosed multiple lesions in the pelvic bones and sacrum. Bone biopsy was read as compatible with adenocarcinoma tubular type. Prostatic acid phosphatase was normal but acid phosphatase was elevated 3x normal; plasma testosterone was 4.3 ng/ml (n3-10). Having failed to identify primary site we began therapy with 3-75 mg D, Trp6 microcapsules. A continuous and steady improvement was noticed manifestied with complete resolution of the clinical syndrome, suppression of T to castrate levels and normalisation to acid phosphatase and resolution of the presacral mass. A 5 yr follow-up has established that the patient has shown a complete response (as per NPCP criteria) and in this respect it is the first case-to our knowledge- after GnRH agonist therapy resembling the original one of Huggins and Huggins described three decades ago.

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RELATIONSHIP BETWEEN TISSUE ANDROGENS AND PROLIFERATIVE ACTIVITY IN HUMAN PROSTATIC CARCINOMA.

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To determine the relationship between intratissue androgen levels and proliferative activity of prostate tumor tissue, the transplantable, androgen dependent, human prostatic tumor line, PC-82 was used. Mice were supplemented with various doses of testosterone (T) resulting in plasma T levels ranging from 0 to 20 nmol/l. Intratissue T and dihydrotestosterone (DHT) levels were measured and proliferation of the tumor tissue was assessed using ki-67 as well as BrdU monoclonal antibodies. A clear correlation was shown between PC-82 tumor growth or intratumor DHT and the percentage of BrdU positive cells ($r = 0.69$, $n = 26$, $P < 0.001$ and $r = 0.80$ $n = 23$, $P < 0.001$, respectively). It was found that a DHT concentration of 3 pmol/g tissue resulted in stabilization of tumor burden, corresponding with a proliferative activity of approximately 2 % of BrdU positive cells, whereas in optimally growing tumors about 5 % of all cells incorporated BrdU. These data will be compared with the ki-67 staining results.

This study was supported by a grant of the Dutch Cancer Society.