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RADICAL PROSTATECTOMY: REPORT ON 30 CASES

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Study material consisted of 30 prostatectomies performed for patients with stage IIB and C disease. The technique utilized consisted in (1) nodal dissection according to the technique of Skinner, and (2) prostatectomy from bottom to top, with 10 urethro-vesical sutures. Results of treatment were as follows: no cases of incontinence, 60% rate of impotence. There was one case of pulmonary embolus, and one retroperitoneal hematoma. There were no deaths. Diagnosis and preoperative staging need to be improved because the disease stage was underevaluated in 30% of cases in view of examination of the surgical specimens.

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RENEWAL TIMING OF LONG ACTING DEPOT LH-RH AGONIST PREPARATION (ZOLADEX) IS CRITICAL FOR A MAXIMAL EFFECT.

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The effects of LH-RH agonist (Zoladex) treatment on hormone dependent rat prostate tumor (R3327H) was investigated based on tumor volume and histology. To this end tumor bearing rats were treated for 10 weeks with Zoladex in depot preparation by implantation every 2, 4 or 6 weeks. Tumor growth rate was similar in the castrated and in the animals treated every 2 weeks with Zoladex. This growth rate was significantly slower than in animals treated with Zoladex every 6 weeks and non-treated group. The growth rate in animals treated every 4 weeks although appeared to be faster it was not significantly different from castrated group. Tumor histology indicated the least amount of surviving cells with acini in the castrated and animals treated every 2 weeks with Zoladex. There was progressive increase in the number of surviving cells in tumors from animals treated with Zoladex every 4, 6 weeks and non-treated animals. Testosterone levels measured during Zoladex exposure support the above observations. These results, obtained for a 10 weeks treatment duration, strongly suggest that careful attention has to be paid to the time of Zoladex renewal in prostate cancer treatment.

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PROSTATIC ACID PHOSPHATASE IN ADVANCED PROSTATIC CANCER (M1)

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Prostatic acid phosphatase (PAP) in serum was used as an aid in monitoring the course following endocrine therapy in a phase III study on metastatic prostatic cancer (M1). PAP levels were measured by radioimmunoassay techniques. All patients in whom PAP levels remained elevated despite treatment died within a year. Re-increase of PAP was an early sign of relapseand in one case a slight elevation preceded the relapse 1-2 months before any other signs were detectable. Thus, in our experience, the high risk patients were identified by PAP measurements. Furthermore, PAP appeared to be a sensitive marker to predict the relapse.

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RELATIONSHIP OF ANDROGEN RECEPTORS TO THE GROWTH AND REGRESSION OF THE PROSTATE

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Since androgen receptors (AR) stimulate growth and block regression of the prostate through direct binding to nuclear sites, androgen withdrawal therapies must effectively eliminate AR from nuclei to bring about regression of prostatic carcinoma. Using this criterion, we compared the effects of surgical castration to 12 different androgen withdrawal regimens on the rat prostate. The most potent treatment in this regard, a combination of cyproterone acetate and low dose diethylstilbestrol, caused an initial objective response rate of 98% in 51 patients with stage D prostate cancer. Thus while assays for AR are useful for evaluating new drugs, the high inital response rates to treatment make them irrelevent for routine patient selection. Accordingly, the principal reason for studying AR is to determine the cellular and molecular processes leading to the eventual emergence of androgen-resistant stem cells. At the cellular level, tumour recurrence in the androgen-dependent Shionogi tumour system is characterized by a 30-fold enrichment of stem cells which possess cytoplasmic AR but which lack the ability to retain AR in the nucleus. While at the molecular level, definitive results await the purification of AR and their genes, the occurrence of biologically-active truncated and chimeric forms of AR, analogous to those which have been synthesized *in vitro* for other steroid-receptors, would predictably yield an androgen-resistant phenotype.