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A COMPARATIVE STUDY BETWEEN DECAPEPTYL - AND ORCHIECTOMY IN THE TREATMENT OF ADVANCED PROSTATIC CANCER.

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In this multicentre study we compare the effectivity of "decapeptyl", a long acting LHRH analogue with orchiectomy. Possible side effects and toxic effects are researched. Sixty-six untreated patients were randomised. All suffered from a histologically proven carcinoma of the prostate at any stage (T,N,M) for which orchiectomy would classically be the treatment of choice. The LHRH treatment consists of monthly I.M. injections of 3 mg decapeptyl ; the surgical procedure used is the pulpectomy. Subjective and objective parameters are followed (micturition problems, bone pain, side effects, complete blood analysis with testosteron levels and acid phosphatases, prostatic volume, metastasis). The mean follow-up exceeds now 15 months.
From the third month on the clinical evolution is completely comparable in both groups, although 25 % of men treated by LHRH improve slower at the beginning ; one case presented a clinical flare up of symptoms. The testosteron levels reach "castration" levels 3 weeks after the first injection. The prostatic volume is equallyreduced and the evolution of the bone metastasis is completely comparable. Side effects, specific for decapeptyl are very few : two patients complain about pain at the injection place and two other devellopped an allergic reaction. No single trace of toxicity could be found up to now. So, both treatments are equally effective and safe, although clinical improvement can be slower with decapeptyl.

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PROTECTION FROM CYTOTOXIC-INDUCED GONADAL INJURY WITH A GONADOTROPIN-RELEASING HORMONE AGONIST (LHRH)

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Introduction: Aggressive chemotherapy (CT) induces gonadal and reproductive dysfunction. Continued supraphysiological administration of LHRH agonist inhibits LH and FSH release and suppresses the spermatogenesis and the testosterone (T) production in men. Using this antifertile effect we treated patients with LHRH agonist during CT in order to protect the germinal epithelium from cytotoxic damage.
Patients and Methods: 14 days before CT with cis-platinum, vinblastine and bleomycin Buserelin (Suprefact^{R}) was administered at a daily dose of 3x0,5 mg s.c. in 4 patients with testicular cancer. During and 14 days after CT Buserelin was given intranasally at a daily dose of 3x0,4 mg. T, LH and FSH were measured by RIA (Serono) twice a week. Sperm analyses were performed before and in a monthly intervall after CT.
Results: LH, T and FSH serum levels were effectively suppressed during pretreatment with Buserelin and remained low during CT. The hormone levels rose to normal values within 4 weeks. All patients were azoospermic 1 month after cessation of CT but showed oligozoospermia 3 months after CT indicating an immediate restitution of spermatogenesis after CT.
Conclusions: 1. T, LH and FSH serum levels were effectively suppressed within 14 days of s.c. administration of Buserelin. 2. The antifertile effect of Buserelin was reversible in all patients indicated by normalization of hormone levels and restitution of spermatogenesis. 3. These preliminary data suggest that the germinal epithelium may be successfully protected from drug induced gonadal toxicity by LHRH agonist.

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GNRH-BINDING-SITES IN HUMAN EPITHELIAL OVARIAN CARCINOMA

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Gonadotropin Releasing Hormone (GnRH) has significant suppressive effects on rat ovaries, where it is bound by high affinity receptors. Recently, we and others found low affinity, high capacity GnRH-binding-sites in both human granulosa cells and corpora lutea (K_a = 4.6 ± 1.9 x $10^5 M^{-1}$, concentration 8 - 150 pM/prot.). Now we studied 6 human epithelial ovarian carcinoma for GnRH-binding: tumor samples were homogenized and incubated for 4 h with 2 x 10^{-10}M ^{125}I D-Ala^6-des-Gly^{10}-GnRH ethylamide and increasing concentrations (10^{-9} - 10^{-4}M) of the unlabelled analogue or native GnRH or other peptides. In three of the tumors tested a binding of the analogue could be detected (K_a = 1.3 - 8 x $10^9 M^{-1}$, concentration of binding-sites: 2 - 85 pM/prot.). GnRH displaced the labelled analogue in the same way as the superagonist itself. No displacement of analogue-binding was obtained with TRH, oxytocin, and somatostatin. These results encourage further studies on the role of these specific GnRH-binding-sites for the growth of human ovarian carcinoma.

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A GONADOTROPIN RELEASING HORMONE (GnRH) AGONIST HAS SPECIFIC BINDING SITES ON NORMAL HAMSTER MAMMARY TISSUE.

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Recent trials have shown that GnRH agonists have some beneficial effects in the treatment of breast cancer in experimental animals and in women. The present experiments were designed to test whether there are GnRH binding sites in mammary tissue (MT) which might at least partially account for the effects on breast cancer. The possibility was examined using ^{125}I labeled D-Ala$_6$ des-Gly$_{10}$ GnRH ethylamide (D-Ala). The procedure was similar to that used for determination of pituitary GnRH receptors (Endo 105:1369,1979). Preliminary experiments indicated that MT from normal cycling female hamsters had binding sites for D-Ala and a significant proportion of this binding was displaceable with 20 pm unlabeled D-Ala (11.7±0.2 M±SE fmol/mg protein total binding, 6.8±0.3 nondisplaceable). Comparably the pituitary glands from these animals had 13.7±0.4 total binding of which 3.7±0.2 was nondisplaceable while the liver and thymus had no detectable displaceable binding. MT from hamsters ovariectomized 1 week earlier had a higher concentration of displaceable D-Ala binding (7.9±1.0 fm/mg protein) than MT from pregnant (3.65±0.3) or lactating (0.7±0.1) hamsters. A competition curve was then performed on MT from ovariectomized hamsters using varying concentrations of unlabeled D-Ala and other peptides. Scatchard analysis of the D-Ala curve resulted in a straight line and the Ka was 1.75 x 10 M^{-1}. 10 pmol D-Ala displaced 80% of the binding whereas 1 nmol of native GnRH, substance P, somatostatin or neurotensin did not displace more than 30% of the binding.

These results indicate that there are specific binding sites for a GnRH agonist analog on normal mammary tissue of hamsters. The hamster mammary tissue may be a useful model system to examine the dynamics of mammary binding sites.