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PROSTATE CANCER.OLD QUESTIONS AND SOME MODERN ASPECTS OF HISTOLOGY AND IMMUNOHISTOCHEMISTRY.
G.Dhom, G. Seitz, N.Wernert
Institute of Pathology, University of the Saarland, 6650 Homburg/Saar, FRG
Histopathologic diagnosis of prostate carcinoma is not yet free of problems even today. There are particular difficulties in demarcating atypical forms of hyperplasia from well differentiated carcinoma and in diagnosing and classifying incidental carcinomas. The accuracy of frozen section detection of lymph node metastases is important for radical prostatectomy. In our own observation material the sensibility is 84%, the specifity 100%. New immunohistochemical techniques give an insight into the receptor content of prostate and show the histogenesis of prostate carcinoma in a new light. The estrogen receptor (modified ERICA test) is evident in the stromal nuclei, fibrocytes, smooth muscle cells and basal cells of the epithelium, but not in the secretory epithelium. The receptor-associated protein - ER-D5 - is found in the cytoplasm of stromal and basal cells. In basal cells and secretory epithelium the keratins show a different pattern. Immunohistochemically common adenocarcinomas display the pattern of secretory epithelium; urothelial and squamous cell carcinomas, on the contrary,the pattern of basal cells. This finding is against the opinion that the basal cell is the stem cell of secretory epithelium and the precursor cell of prostate carcinoma.

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PHARMAKINETICS STUDY IN MAN OF D-Trp-6-LHRH (DECAPEPTYL, Ipsen-Biotech) ADMINISTERED AS SLOW RELEASE MICROSPHERES
K.Drieu[1],J. Devisaguet[2], F. Dray[3], E. Ezan[3]
1-IHB, 92350 Le Plessis Robinson; 2-Fac. de Pharmacie, 92290 Chatenay Malabry;3-URIA INSERM U.207, Institut Pasteur, 75015 Paris, France
A specific, sensitive (70pg.ml^{-1}) radioimmunoassay developed for D-Trp-6-LHRH allows measurement of blood levels of this peptide in man after injection of the simple form (0.1mg subcutaneous) or the slow release form (3.75mg im). Pharmacokinetic parameters for the simple form injected subcutaneously (0.1mg Decepaptyl) were measured in 6 healthy controls and 10 patients. After a plasma peak at around 1 hr (approx 1.40 to 1.80ng.ml^{-1}) and a distribution phase of 3-4 hr, the elimination half-life was 7.6$\pm$1.6 hr in controls, 11.8$\pm$3.1 in pts. Plasmatic clearance was longer in pts, perhaps due to their age and general condition. Biodegradable, biocompatible microspheres (ms) (3mg Decapeptyl dispersed in a porous matrix) release the active principle regularly over 1 mo., ensuring the blood levels needed for biological effect. After im administration of ms to 10 pts, an initial peak was seen, probably due to release of the active principle on the periphery of the ms; concentrations then stabilized beginning at 24hr, creating a plateau lasting 4 wk. Average concentration at equilibrium was 0.32$\pm$0.09 ng. ml^{-1} and inversely proportional in each subject to plasmatic clearance. The stability of individual levels reflects the rate of D-Trp-6-LHRH release from its polymer support.

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A PHASE II TRIAL OF CHEMOTHERAPY (CT) WITH FLUOROURACIL (F), DOXORUBICIN (A) AND CIS PLATIN (P) IN ADVANCED PROSTATIC CANCER (APC)
J.P. Droz, H. Lupera, G. Piot,
P. Laplaige, M. Ghosn, C. Théodore.
Institut Gustave-Roussy - Villejuif, France
From october 1985 through december 1986, 25 patients (pts) with APC entered in a phase II trial CT with F 600 mg/sqm/d, dl,2 - A 40 mg/sqm/dl and P 90 mg/sqm dl every month.
The measurable disease was : prostate 15 pts, bone 20 pts, lung 6 pts, liver 5 pts, lymph nodes 4 pts, others 2 pts. In 21 pts Prostatic Acid Phosphatase were normal in 5, elevated in 16.
The response was evaluated after 3 cycles of CT according to the National Prostatic Cancer Project criterias. There were 0 CR, 1 PR, 13 stabilizations, 11 progressions.
Toxicity (T) was assessed using WHO criteria. Alopecia and vomitings were universal. There were : 11 grade 1 anemia and 2 aplasia, 1 grade 1 renal T.
FAP CT appears to have marginal effect in APC.

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ON OPTIMATION OF REFERENCE VALUES FOR PROGNOSTIC MARKERS.
P.Ekman, A.Lewenhaupt, P.Eneroth, and A.Kallner
Karolinska Hospital, Stockholm, Sweden.
Introduction: Markers reflecting the biological activity of a tumor should be of great importance for an individualised therapeutic approach in prostatic cancer. The selection of upper normal limits is routinely based on data from a healthy normal population. Little attention has been paid to the degree of elevation as such.
Methods: Sera from 83 patients with prostatic cancer was collected at the time of diagnosis and analysed with regard to content of prostatic acid phosphatase (PAP), neopterin, and osteocalcin. The data were related to survival after two years. The efficiency of each test, at different cut off levels, to predict cancer death within two years was calculated by statistical means.
Results: The standard cut off level for PAP, 1.9ug/l, was a poor prognostic parameter. Not until the level was raised to 20ug/l the efficiency was over 80%. At a cut off level for neopterin of 8nM/l, 74% survived beyond 2 years compared to 43% at 12nM/l. The corresponding figures for osteocalcin at 3 and 7ug/l were 79% and 20% respectively. For both these markers an adjustment to a higher cut off level could be made without increasing the number of 'false negatives'. At the recommended cut off level, 5ug/l, osteocalcin had an efficiency of over 85%.
Conclusion: An elevated level of a tumor marker often reflects a poor prognosis. Additional information can be gained when also the degree of elevation is taken into account.