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11.103

HEPATOCELLULAR CARCINOMA (HCC): TOPOGRAPHIC STUDY.

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To investigate whether HCC has a preferential distribution among hepatic segments, abdominal ultrasounds of 331 patients with HCC (245 M, 86 F; 70 HBsAg+, 92 heavy drinkers) were evaluated; 255 had also liver cirrhosis. HCC was solitary in 63% of cases, multifocal in 26%, diffuse in 8% and massive in 3%. In cirrhotics, massive HCC was only found in HBsAg+ subjects (P=0.005). The prevalence of HCC types was not influenced by gender, age, alcohol intake, presence of cirrhosis and histological grading. Right lobe was involved in 90% of cases, left lobe in 31% (both lobes in 25%) and caudate lobe in 3% (P<0.001). The involvement of the segments was specified in 275 patients:

SEGMENT	CIRRHOSIS	NON-CIRRHOSIS	P*	P**
I	4 (2%)	0	ns	Total: <0.001
II	37 (17%)	12 (21%)	ns	Cirrhosis:<0.001
III	48 (22%)	15 (26%)	ns	Non-cirr.: <0.001
IV	53 (24%)	18 (32%)	ns	
V	50 (23%)	23 (40%)	0.012	
VI	67 (31%)	25 (44%)	ns	
VII	91 (42%)	24 (42%)	ns	
VIII	48 (22%)	13 (23%)	ns	

* for differences in prevalence between cirrhotics and non-cirrhotics.

** for differences in prevalence between segments.

Analyzing solitary HCC, segment VII (35%) was again the most affected (P=0.001) and, in non-cirrhotics, segment V was often involved (36%) too. This distribution was not influenced by any of the previous parameters. In cirrhosis, massive HCC is more frequent in HBsAg+ carriers. HCC has a preferential distribution with maximal prevalence in segment VII and minimal in segment I. Segments V and VI are also frequently involved in non-cirrhotic liver.

11.104

FLOW CYTOMETRICALLY (FC) DNA/TOTAL PROTEIN CONTENT AND CELLULAR HETEROGENEITY IN HUMAN LUNG TUMORS.

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DNA and total protein measurements have been performed on cells from neoplastic and non-neoplastic lung sample from 104 patients, with the aim of describing neoplastic cells and their cycle in more detail and with the porpose of reaching a better discrimination of normal and malignant cells. Biparametric analysis demonstrated that cells with abnormally high red fluorescence (i.e. protein content), which is indicative of unbalanced growth, were often observed in malignant tumor with respect to normal lung samples. Furthermore, the dual parameter analysis allowed the recognition of additional aneuploid tumor cell lines, thus indicating that the frequency of cytometrically diploid tumor is lower than that previously described by DNA monoparametric analysis. The recognition of aneuploid subpopulations by dual parameter analysis in clinically- and histologically-negative one-parameter flow cytometric "diploid" samples assumes an important diagnostic value. The results have also shown the presence of multiple protein subpopulations in clones with the same ploidy value, thus indicating a higher level of cellular heterogeneity than demonstrated by DNA monoparametric measurements. In conclusion, DNA/protein biparametric measuraments may significantly contribute to the diagnostic and prognostic assessement of human neoplasia.

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11.105

Free microvscular tissue transfers in head and neck reconstruction

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Defects after head and neck cancer surgery constitued the main indication for use of microvascular free tissue transfer for reconstruction.

Betwen january of 1989 and march of 1991 seventy-one patients underwent free tissue transfers for head and neck defects in cojunction with or after major ablative surgery. All patients had diagnosis of malignancy. Sixty four patients had a histologic diagnosis of squamous cell carcinoma. In the seven remaining patients, there were fife bazal cell carcinomas, two malignant melanomas.

In this series of seventy-one patients the original site of tumor was oral cavity in 17, the oropharynx in 5, the lower lip in 14, the larynx in 11, the hypopharynx in 9, the skin in 15.

There were 20 myocutaneous flaps, 32 fasciocutneous flaps, 2 osteocutaneous flaps, 3 bippadled latissimus dorsi and scapular flaps, 6 free bowel autografts, 7 omental flaps, and one bippadled stomachal and omental autograft. Free tissue transfers was succesful in 63 of 71 cases / 89 percent /.

11.106

A PHASE II STUDY OF OCTREOTIDE IN METASTATIC ADVANCED PROSTATIC CANCER (MAPC).

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Octreotide, a long-acting somatostatin analogue, has demonstrated in vitro ability to inhibit the growth and the cell differentiation of various tumors. Our preliminary results (E.J.Canc.Clin.Onc.26:186, 1990) have evaluated the inhibitory effects in MAPC either alone or with LNRH antagonist. The action's mechanism of octreotide may be mediated through a inhibition of growth factors (EGF,FGF), somatotrophins (PRL,GH) and a direct antiproliferative effect. We started a phase II of study about octreotide in twelve patients (pts) with MAPC to assess its activity. The pts, median age 68 years (range 58-79) have measurable disease and secondary pain to cancer. All the pts have been treated with 0,1 mg/mq tree time a day for 4 weeks. The results of this work show that all pts have a discount of pain, 3/12 have a 50% reduction in analgesic use. The side effects were very low with hot flushes in 2 pts and aching in the inoculation point in all pts. In conclusion these data demonstrated that octreotide terapy is efficacious for the reduction of pain and future pts must be treated for a longer time to a final assessment of tumor response.

11.107

GROWTH INHIBITORY EFFECTS OF COMBINED TREATMENT WITH LEVAMISOLE AND 5-FU ON HUMAN COLORECTAL ADENOCARCINOMA GRAFTED IN NUDE MICE

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In an attempt to develop a reliable animal model that closely mimics the clinical adjuvant setting, fragments of human colorectal adenocarcinomas were inserted under the renal capsule of nude mice.

Intraperitoneal treatment with levamisole, 5-FU or 5-FU combined with levamisole was initiated with an alternating regimen. A 4-day course of 20 mg/kg 5-FU was followed by a 3-day course of 2.5 mg/kg levamisole. This schedule was repeated 3 times in the two first experiments and 2 times in all the subsequent trials. In 7 out of 9 experiments, the combined use of 5-FU with levamisole induced regression of the tumor transplants while both compounds given as monotherapy had no effect. Closer observations of the results revealed that the combined administration of 5-FU and levamisole was effective (growth inhibition of 33-59%) in all the experiments where the control fragments did grow. In one trial with decreased control implants, the number of completely disappeared fragments (6 out of 10) in the 5-FU/levamisole treated group was much higher than in the saline (2 out of 9) or levamisole (1 out of 10) treated groups. In two trials, control fragments failed to grow and neither therapy had any effect.

These data demonstrate that combination of levamisole and 5-FU inhibits the growth of human colorectal adenocarcinoma in nude mice and suggest that this model could be useful to further investigate the use of levamisole in other oncologic settings.

11.108

EXPERIMENTAL AND CLINICAL STUDIES WITH R75251: AN ANTITUMORAL AGENT WHICH INHIBITS RETINOIC ACID (RA) METABOLISM

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R75251 is an imidazole derivative which inhibits several P450-dependent enzymes, ie the aromatase, the 17-hydroxylase and the 4-hydroxylase of the catabolic pathway of retinoic acid (RA). The antitumoral activity of R75251 has been demonstrated in patients with metastatic prostate cancer who had relapsed after orchiectomy. Side-effects were mainly related to benign cutaneous reactions, resembling those of hypervitaminosis A. The drug does not have in vitro cytostatic properties, as measured by cell proliferation in various tumour cell lines. It does not show any retinoid-like properties but R75251 enhanced the cell differentiation and plasminogen activator production induced by RA in F9 teratocarcinoma cells. R75251 also increased the inhibiting effects of RA on MCF-7 cell growth in culture. In rats, after oral administration of R75251 the endogenous RA levels rose both in tumors and in plasma. In rats, R75251 reduced the growth of established androgen-dependent rat Dunning G and H prostatic adenocarcinoma when treatment was initiated at a tumor volume of 0.25 cc . It also reduced the growth of H tumors if treatment was initiated when tumors relapsed after castration. A 50% reduction of tumor volume was also shown in the androgen-independent Matlu, H* and PIF-1 sublines. The growth of TA3 mammary carcinoma in Swiss mice (a steroid independent mammary carcinoma) and Dunning G prostate carcinoma in nude mice were also inhibited by both R75251 and RA.

It is concluded that antitumoral properties of R75251 may be related to inhibition of RA metabolism.