Symposium no. 6: Environmental Carcinogens and Relevance to Humans

6.019

Mycotoxins in cereal samples from an area with Balkan endemic nephropathy and urinary tract tumours in Bulgaria.

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Home-produced cereals collected from endemic and non-endemic regions in Bulgaria were analysed for the content of carcinogenic ochratoxin A and other mycotoxins in relation to the hypothesis for the possible involevement of some mycotoxins in the etiology of Balkan endemic nephropathy and urinary tract tumours

6.020

MOLECULAR EPIDEMIOLOGY IN THE PREVENTION OF OCCUPATIONAL CANCER, WITH SPECIAL REFERENCE TO ASBESTOS EXPOSURE.

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The promotional phase of carcinogenesis (C) is reversible and its timely recognition would open the way to efficient preventive interventions. Molecular epidemiology has identified a series of markers (e.g. oncoproteins, enzymes) characteristic of this phase; for instance the presence, in the serum, of the p21 ras oncoprotein has been considered to be a consequence of carcinogen exposure and a sign of increased risk. We have shown carcino-embryonic antigen (CEA) to be a marker of C (15th Int. Cancer Congress, 1990, abstract n° 145.01) of which the expression is related to some well-defined mechanisms of C (presumably chemical C). Free radical C., as after exposure to asbestos, and mesothelioma, are characterized by overexpression of Tissue Polypeptide Antigen - a cytoskeleton marker - and possibly Ferritin, whereas CEA is not expressed. However the latter becomes expressed when the association with smoking induces bronchogenic carcinoma of NSCLC type, and enolase when SCLC is induces. These changes in the serum marker levels are early events during the C process and shed light on its mechanism and - predictively - on its outcome; they open new perspective for specific prevention by interfering with the different C mechanisms. This approach has been applied to workers exposed to asbestos, to nickel and chromium oxides, to miscellaneoux chemicals, and to subjects dwelling near polluting waste-dumps.

6.021

MESOTHELIOMA REGISTRATION IN BELGIUM

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Founded in 1982, the Belgian Mesothelioma Register meets regularly. New cases are admitted either by pathologists, either by the Found of Professional Diseases. Up to now, 302 cases are registred. Applying routine staining and immunocytochemistry, the interpretation is performed according to the International Mesothelioma Panel, founded by the EEC. A distinction is made in chronic fibrous pleuritis (n = 8), atypical mesothelial hyperplasia (n = 6), benign fibrous mesothelioma (n = 3), malignant mesothelioma epithelial type (= 120), malignant mesothelioma biphasic type (n = 79), malignant mesothelioma desmoplastic type (n = 12) and metastatic infiltration (n = 74). Males around the 6th decade are preferentially affected. An asbestous exposure could be withold in only 60 %. The pleura is in 91 %, the peritoneum in 6 % and the pericardium in 2 % the site of origin. The immunocytochemical analysis of the registered cases reveals a monoexpression for cytokeratin or vimentin in the epithelial type, a coexpression for both intermediairy filaments in the biphasic type in the anaplastic areas and coexpression for the desmoplastic type in only 50 % of the cases. None reveal a strong CEA reaction for the polyclonal antibody, whereas a weak staining is observed in 6 cases.

6.022

OVAL CELL PROLIFERATION : A COMMON ORIGIN FOR REGENERATION AND NEOPLASIA IN HUMAN AND RAT LIVER

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The process of liver cancer development in humans and in experimental animals displays similar pathways. Current theories about hepatocarcinogenesis suggest that neoplastic transformation originates from dedifferentiation of mature hepatocytes or from abnormal differentiation of precursor cells. We are especially interested in the second part of the hypothesis dealing with the abnormal differentiation of precursor cells, the so-called oval cells. Well known in experimental conditions in animals, their occurrence in human liver pathology is considered to be controversial.

We compared the ultrastructural features lasting the different periods of the TAA-induced livercarcinogenesis in rats and human liver biopsies in conditions of chronic cholestasis and neoplastic transformation (cholangiocarcinoma, hepatoblastoma).

Oval cells are the target cells in the TAA model. These cells eventually undergo malignant transformation. In the cholangiocarcinoma the oval cells display a hepatocytic and cholangiocellular phenotype.

In human cholestatic livers identical so-called oval cell proliferations are found. Cholangiocarcinomas and hepatoblastomas reveal proliferations of cells identical to the neoplastic variant of the oval cells in rats.

6.023

Tobacco smoking and lung cancer: presence of PAH-DNA adducts in lung cancer patients.

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It is now generally accepted that tobacco smoking is one of the main causes of lung cancer. Polyciclic Aromatic Hydrocarbons (PAH) contained in tobacco covalently bind to DNA leading to the formation of PAH-DNA adducts. Such binding is a crucial step on chemical carcinogenesis.

Using the ELISA test we have studied 39 DNA samples from peripheral blood lymphocytes of lung cancer patients. There were 53% positive results for PAH-DNA adducts: 14 of these patients were smokers, 6 exsmokers and 1 non-smoker.

The results of this ongoing study could add more informations on the correlation between tobacco smoking and lung cancer.

6.024

DIFFERENTIAL PROMOTION IN LIVER CARCINOGENESIS BY CHOLINE IN FEMALE AND MALE RATS

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Phospatidyl cholines (PC) are the major component of membrane phospholipids. The content of liver microsomal PC, drug metabolizing enzymes and surface of smooth endoplasmic reticulum (SER) membranes are known to be lower in female than in male rats. Choline given to female rats has been found to increase the biogenesis of SER surfaced membranes as well as the enzyme activities and PC content. We studied the effects of a choline-enriched diet given to rats for three weeks during the tumor promotion on the carcinogenic process. The growth of focal lesions after methylnitrosourea as initiator and acetylaminofluorene-CCl_4 as promoters was lower in female rats than in males. The choline-enriched diet stimulated the development of enzyme-altered foci in females but not in males, probably by enhancing the synthesis of PC and SER membranes with an enrichment of lecithin-dependent drug metabolizing enzymes.