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Lung cancer and smoking among men in South India
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Background: About 40% of the males aged 35 and over smoke in Chennai and lung cancer incidence rates are increasing in Chennai over the years. Method: A case-control study on lung cancer to evaluate the role of cigarette and bidi smoking was conducted with 778 cases and 3430 controls in two centers in South India in collaboration with IARC. Results: The odds ratio (OR) and 95% confidence interval (CI) adjusted for age, educational level, center and alcohol habit for lung cancer among ex-smokers and current smokers were 2.4 (1.7-3.3) and 5.4 (4.1-6.9) respectively. Among current smokers smoking cigarettes and bidis were associated with an adjusted OR (95% CI) of 2.2 (1.8-2.7) and 3.8 (3.1-4.8) respectively. The risk increased with duration of smoking habit and daily and cumulative lifetime smoking. An excess risks of 30% and 60% were associated with every 10 pack-years smoked among cigarette and bidi smokers respectively. Compared to current smokers, ten year after stopping smoking habit the risk of developing lung cancer among ex-smokers decreased to 40% and after 15 years to 30%, increased risk of lung cancer was seen among those drinking locally prepared alcohol [OR(95% CI): 1.7 (1.3-2.3)]. No association was seen with chewing tobacco. No interaction effect was seen between habits. Conclusion: Higher risk for lung cancer was seen among bidi smokers than cigarette smokers. Stopping smoking works.

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Immunologic and other biological parameters as a function of smoking status and of residence in areas differing in terms of air pollution
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Our objective: to assess whether residence in a more polluted area was associated with differences in hematological or immunological parameters and serum carcinoembryonic antigen (CEA) level. The old industrial region of La Louvière (Belgium) comprises the urban “La Louvière-Steelworks” area harboring big steel works, semi-urban “Power plant-Landifl” area containing an old style landifl, a coke oven and a power plant fueled with coal and a “Peripheral” area containing rural and semi-urban zones but no important sources of emissions. Method: Biomonitoring study on 293 healthy residents without important occupational exposures. Smoking status was taken into account. Results: Smokers were found to have significantly (p≤0.05) higher absolute numbers of leukocytes, neutrophils, CD3+ lymphocytes (lyns), CD4+ lynos, CD25+ lynos, higher CD4/CD8 ratios and higher CEA levels but significantly lower IgE immunoglobulin levels than non-smokers. Compared to persons living in the “Peripheral area” ±, and after correction for sex, smoking status and age, persons living in the more polluted “Power plant-Landifl” and “La Louvière-Steelworks” areas showed significantly more CD3+CD56+ lynos. Also, persons residing in these areas tended to have less platelets, more lymphocytes. CD3+ lynos, CD8+ lynos, a higher complement C3c serum concentration and a slightly higher CEA serum concentration. Although about the same mean value for the CD4/CD8 ratio was found for the more polluted areas, a higher percentage of their residents showed a ratio that was either <1 or ≥ 2.25. The number of CD3+CD56+ lynos showed a negative correlation with the CD4+/CD8+ ratio (R² = 0.132, p<0.0001). Conclusions: Several parameters studied seemed to be affected differently by smoking and residence in a more polluted area. CD3+CD56+ lymphocyte counts, reported to be increased in cancer patients, were higher in residents of more polluted area’s and showed a negative correlation with the CD4+/CD8+ ratio.

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Breast cancer public organization’s activity features in Ukraine
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Study of breast cancer patients (over 5000) in the Ukrainian Mammology Center revealed some peculiarities in the problem of breast cancer in Ukraine: lack of screening program, deficiency of modern mammograms etc. Presence of our representatives on the First World Conference on Breast Cancer (July 1997, Kingston, Canada) stimulated establishment of All-Ukrainian public organization “Donna” aimed on moral and psychological support for women breast cancer survivors. In 1999 this organization became the member of UICC, thus extending horizon of their activity. Urgency of “Donna’s” activity in Ukraine is increasing each year because of growing number of breast cancer patients, raising death-rate, influence of Chernobyl accident after-effects, active alcohol drinking and tobacco smoking, consumption of large amounts of animal fats, disharmony and incongruity of sexual life and intimate relations as a result of worsening of the income in families and growth of stressful pressure. Based on this the main risk factors for Ukraine can be determined as following: 1. After-effects of Chernobyl accident; 2. Consumption of animal fats; 3. Growth of sexual disharmony leading to hormonal disorders. Activity of “Donna” is aimed on reduction of influence of these factors by means of lectures, talks, publications in mass-media, cooperation with scientific-research institutions. Only three years later the results of this activity are appreciable. Having an example of similar UICC organizations all over the world, members of Ukrainian “Donna” get liberated, and feel themselves able to overcome all hardship and survive in existing situation.

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Molecular follow up of preneoplastic lesions in bronchial epithelium of former Chernobyl cleanup workers
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Irradiation is a potent carcinogen, but the precise molecular damage associated with it is still unknown. In this study we investigated cancer-related molecular abnormalities including K-ras mutations, p53 expression, promoter hypermethylation and microsatellite alterations at seven chromosomal regions in successive biopsies obtained from former Chernobyl cleanup workers in comparison with smokers and nonsmokers who have never had
radiation exposure. Our results indicate that prolonged persistence of inhaled radioactive particles is associated with appearance of alellic loss at 3p21, 3p14.2 (FHT), 3p21, 3p22-24 (hMLH1) and 9p21 (p16NCK1) in bronchial epithelium of former Chernobil cleanup workers. The prevalence of 3p14.2 alellic loss was associated with decreased expression of the FHT mRNA in their bronchial epithelium in comparison with control group of smokers. During several years of our monitoring samples of lung epithelium were collected from the same area of lung. In epithelium exposed to carcinogens (tobacco smoke and/or radioactivity) the total number of molecular abnormalities was significantly higher in dysplasia and in morphologically normal foci progressed later to dysplasia than in these samples which never showed evidence of such progression. Our findings indicate that extensive cancer-related molecular abnormalities sequentially occur in radiation damaged bronchial epithelium of former Chernobil cleanup workers.

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Effect of oligoelements Se, Zn and Mn plus lachesis muta on pancreas cell line growth. In-vitro and in-vivo studies

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The objective of this study was to investigate in-vitro and in-vivo the molecular mechanism of action of Zn, Se, Mn plus L-Muto (LMA) employing a cell line from human pancreatic carcinoma.

Methods: 1.PANC-1 cells were used to determine the effect of LMA on proliferation. Cell cycle was studied by VEA and apoptosis by DNA fragmentation flow cytometry and cell morphology. PCNA and c-FOS proteins were studied by immunohistochemical methods. 2. Three different groups of nude mice (n=10) were injected with 3x10⁶ cells; A: Control; B: pretreated, received daily 0.02 ml of L-MUO beginning 30 days previous to cell inoculation; C: treated, animals received daily 0.02 ml of L-MUO, beginning when tumors attained a diameter of 0.6 cm and continued till the spontaneous death. Tumor growth characteristics, expression of c-FOS and PCNA proteins and survival were analyzed in all groups.

Results: In vitro results showed a significant inhibition (60%) on cell proliferation. Cell cycle analysis indicated an increased number of cells in G2/M phase 48 hrs after treatment. No significant apoptosis was observed with any of the techniques. PCNA was highly expressed in proliferating control cells compared to treated cells; c-FOS showed similar levels in all cells indicating that it is deregulated. 2. The inoculation of nude mice produced the development of semi differentiated ductal carcinomas with the following values in group A, B and C, respectively: Tumor incidence (%): 80, 70 and 80 (p<0.001); X2 test: B vs A and C, latency period days: 10±2, 23±6 and 10±2 (p<0.001); B vs A and C, Newman-Keuls); survival median days: 80, 101 and 128 (p<0.001 logrank test). Tumors from treated animals showed a low expression of PCNA with extensive areas of necrosis.

Conclusions: L-MUO shows in vivo and in vitro a significant inhibitory effect on cell proliferation in agreement with previous reports and with the prolonged survival rates observed in advanced pancreatic cancer patients.

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Morbidity from lung cancer in the Republic of Macedonia - epidemiological study

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Background: In the FYROM, in the last twenty years, malignant neoplasms, especially of the lung, were on the increase. The high mortality from lung cancer was on the second place in the structure of causes of death, after the cardiovascular diseases. Lung cancer is the most common form of cancer in the world. In FYROM, this type of cancer was on the first place among ten most common primary locations of cancers in the year 1997, with the age-standardized rate of 128.3/100,000. Lung cancer continues to be the leading cause of cancer deaths among men in most countries, also in Macedonia, among men, the age-standardized rate was 128.3/100,000. Among women, this type of cancer was on the sixth place, after cancer of breast, reproductive organs, skin and gaster. Female rate was lower (108.4/100,000). The AIM of this study was to analyze the distribution of lung cancer among patients with this disease according to these characteristics: sex, age and place of residence.

Methods: The study includes patients with lung cancer, registered in the Cancer Registry of Macedonia, in the period between 1995-1997. Total number of cases was 2245. Data were examined with descriptive and analytical epidemiological methods.

Results: During the observed period (1995-1997), morbidity dynamic shows rates of 37.3/100,000. According the frequencies by sex, the distribution is significant between men and women (X2=1164; DF=2;p<0.001). Analyses of morbidity by sex and age during the observed period shows the highest rate in men at the age group between 70-74 years, when it was 463.8/100,000 population (in the year 1997). Among women, the highest morbidity rate was observed in 1995 (78.8/100,000), at the age group between 75-79. Distribution by sex and place of residence shows that in both sexes, most of the patients were from urban area (men 76.7%; women 59.5%). Conclusion: The results of this study show that lung cancer in the Republic of Macedonia takes an important role in cancer morbidity. During the observed period (1995-1997), men were 5 to 6 time folds more often ill. Among both sexes, lung cancer appears most frequently at the age group between 60-79 years.

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Texas cancer plan - 15-year report card

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In the 1980s, the Texas State Health Department projected that between 1985 and 2000 the number of new cancer cases in Texas would increase by more than 85%. The Texas State Legislature responded by appointing a citizens task force to develop short-term and long-range action plans to reduce cancer mortality in the state, and created the Texas Cancer Council (TCC) to implement this plan. Seed funding was provided from the state budget (taxes). Existing agencies and organizations served as the building blocks to construct a statewide program. The Texas Cancer Plan, Actions and Directions for the Future, 1985 to 2000 served as a blueprint for action. Improved incidence data collection, inventory of and expansion of cancer resources, improved cancer information data systems, implementation of comprehensive school health programs emphasizing cancer prevention, expanded cancer screening, and training nurses, physicians, dentists and medical students in cancer prevention, screening and early detection were undertaken.
Expression of pancreatic duodenal homeobox gene-1 in pancreatic cancer and its correlation with clinicopathological factors

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Introduction: The original cells responsible for generating pancreatic ductal adenocarcinoma remains unclear. In the pancreatic regeneration, pancreatic duodenal homeobox gene-1 (pdx-1) emerges in ductal cells that have pluripotency to differentiate into islets. Therefore, pdx-1 is thought to be a marker of de-differentiated cells to regain their pluripotency to differentiate into any pancreatic cell type. In this study, we analyzed pdx-1 expression in pancreatic cancers and its correlation with clinicopathological factors. Methods: We examined 35 patients with pancreatic cancer who had undergone resection at our institution between 1994-2000. Immunohistochemical staining was performed by the immunoperoxidase technique. Correlation with pdx-1 expression, tumor size, TNM stage, tumor grade and tumor pathology were investigated with the use of the chi-squared test. Kaplan-Meier method was used to calculate survival curves and Log-Rank test was performed to compare differences in survival rates. The influence of various clinicopathological factors on overall survival was also assessed by Cox’s proportional hazard model. Results: Fifteen of 35 pancreatic cancers (43%) were positive for pdx-1 expression and 20 (57%) were negative. Among the clinicopathological factors, microscopic lymphnode metastasis and histological grade significantly correlated with pdx-1 expression (p = 0.02 and 0.04, respectively). Patients with positive pdx-1 expression tended to show less lymphnode metastasis and higher histological grade. Further, patients with positive pdx-1 expression had a significantly worse survival than those with negative (p = 0.02). By means of Cox’s proportional hazard models, univariate and multivariate analyses revealed that pdx-1 is an independent variable affecting overall survival (p = 0.03). Conclusions: This study suggests that pdx-1 may play an important role in the progression of pancreatic cancer. Its value to predict prognosis remains to be determined.

Surgical resection for noninvasive and invasive intraductal papillary mucinous carcinoma

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The background of the study: Intraductal papillary mucinous tumor of the pancreas is a recently established clinical entity which includes a spectrum of lesions ranging from benign adenoma to malignant infiltrating carcinoma. Patients with intraductal papillary mucinous adenoma have a favorable prognosis after surgical treatment. However, recurrent disease frequently occurs in patients with invasive intraductal papillary mucinous carcinoma. The clinicopathological, imaging, and prognostic differences among adenoma, noninvasive carcinoma and invasive carcinoma have not been clarified.

The method used: Between June 1995 and December 2001, 29 patients with intraductal papillary mucinous tumors of the pancreas underwent surgical resection at the National Cancer Center Hospital East. They were divided into three groups: adenoma (n = 10), noninvasive carcinoma (n = 9), and invasive carcinoma (n = 10). This single-institute study examined the imaging findings, histopathological features, and outcome after surgical resection in patients with intraductal papillary mucinous tumors.

The results obtained: The median size of adenoma, noninvasive carcinoma, and invasive carcinoma was 3.3cm, 5.0cm, and 5.7cm, respectively. There was a significant difference in size between adenoma and carcinoma (p = 0.006). All patients with adenoma or noninvasive carcinoma were alive without recurrent disease. In cases of invasive carcinoma, 70% had lymph node involvement and 80% had retroperitoneal invasion. The 1, 2, 4-year actuarial survival rate for patients with invasive carcinoma was 39%, 26%, 13%. Recurrence occurred as liver metastasis in 3 patients, carcinomatous peritonitis in 3, local recurrence in 3, and lung metastasis in 1.

The conclusion reached: Patients with adenoma or noninvasive carcinoma had a better prognosis than patients with invasive intraductal papillary mucinous carcinoma. Margin-negative pancreatic resection can be recommended for treating invasive carcinoma.

Plasmacytoma of pancreas: a case report

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Secondary plasmacytoma is a malignant extravascular proliferation of plasma cells common for multiple myeloma (MM) in advanced stages. Here we present a case of Plasmacytoma of the pancreas. An 82-year-old female with a history of MM (lgA Lambda) diagnosed in Jan 2000 and who was being treated with melphalan and prednisone came in Dec 2001 with complaints of weakness and back pain. Physical examination was remarkable for jaundice; there was no hepatomegaly or abdominal mass. Laboratory studies showed a hemoglobin of 9.4g/dl, BUN of 12mg/dl, creatinine of 0.9mg/dl, calcium of 10.2mg/dl, total bilirubin of 18.3mg/dl, direct bilirubin of 12.9mg/dl and alkaline phosphatase of 537u/l. Hepatitis profile was negative. Right upper quadrant sonogram showed mild intra hepatic biliary ductal dilatation. CT scan of abdomen showed multiple soft tissue densities in pancreas, portahepatis, adjacent to right kidney and dilatation of intra hepatic bile ducts. ERCP was performed and stent was placed in the common bile duct. The total bilirubin dropped to 3.0mg/dl in 6 days. CT guided biopsy of the mass was done and it showed plasma cells. We had planned to give radiation therapy to the area. The most common sites of extraosseous myelomatous infiltration are the liver, spleen and lymph nodes. It is unclear as to why these tissues are more prone to Plasmacytoma than others. Plasmacytoma of pancreas is a very rare condition. When a pancreatic mass is detected in a patient with previously diagnosed MM Plasmacytoma should be suspected, as it is sensitive to radiation.
Novel treatment for advanced pancreatic cancer, 73 patients 10 years follow up

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Background: Pancreatic carcinoma (PC) is highly resistant to chemotherapeutic agents (CHT). The most commonly used CHT have very poor response rates even and very low median survival rates (MSR). Several toxic effects are present. Previous results obtained prolonged MSR free of side effects in colon carcinoma. PC and mammary carcinoma, lead us to carry on this trial using the association of low dose Lachesis Muta venas and trace elements Se, Zn and Mg LMO.

Method: A group of 73 patients entered the experiment. The eligibility criteria were: non resectable advanced local or meta- static PC, post surgical relapsed PC, histological confirmation, previous therapy suspended 3 weeks prior to the beginning of our treatment, ECOG status 0 to 3, life expectancy 12 weeks, icteria, bone marrow hipofunction and hepatic enzyme alterations were allowed if not compromising life expectancy. Patients were treated with daily intramuscularly applied 5 cm3 during all the follow up.

Results: The 73 patients that entered the test showed a 19 months MSR (578 days) 25% of them were alive five years later. Absolutely no secondary or adverse effects were observed due to the treatment. Remission of tumor masses was rarely observed but stabilization during long periods and slow increase was observed. Patients with relatively big metastatic or primitive tumor masses were able to carry on almost normal activities (ECOG 1/2) until the latest weeks of survival. Important quality of life benefits were observed, due to the absence of adverse effects and psychical improvement compared with previous CHT treatment periods, in the same patients. Advanced PC patients showed MSR duplicating those obtained with the latest CHT, without toxic or undesirable effects.

Conclusion: We consider the LMO treatment highly recom- mendable for PC patients in any stage in place of CHT drugs and as a complementary therapy associated to radiotherapy, surgery and CHT.

Effect of an energy and protein dense, high n-3 fatty acid oral supplement on tumor response in patients with cancer cachexia


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Background. Eicosapentaenoic acid (EPA), an n-3 fatty acid, has been shown to have anti-cachectic and anti-tumor properties. Previously, a net gain of body weight and lean body mass was demonstrated with an intake of 1.5-2 cans/day of an energy and protein dense, high EPA and antioxidant oral supplement in patients with advanced pancreatic cancer. In the present study, the effect of this supplement on tumor progression was evaluated.

Methods. An 8-week multicenter, randomized, double-blind trial enrolled 200 cachectic patients with pancreatic cancer. Patients were randomized to consume 2 cans/day of the experimental (E95) or control (C105) supplement (480mls, 620kcal, 32g protein ± 2.2g EPA). Plasma phospholipid EPA (pEPA) levels were measured by gas chromatography and serum CA19-9 levels were assessed by ELISA at baseline and 8 weeks. Non-parametric tests were used for within- and between-group comparisons of change in CA19-9 levels from baseline to week 8. Correlations between change in pEPA and CA19-9 levels were examined. Results. 110 patients (50E:50C) completed the 8-week study. CA19-9 levels increased over the 8-week study in both groups (p<0.001). There was no significant difference in the change in CA19-9 levels between groups; median change (range) E: 205 (415) to -1395 (50). There was no significant correlation between the change in CA19-9 and pEPA for either group. Nonparametric Two Way ANOVA demonstrated no significant interaction between the stage of disease and treatment group, however, patients with stage IV disease had a greater increase in CA19-9 levels over the study period than patients with stage III/III, median change stage III/III, stage IV: 1470, p = 0.001

Conclusion. This study suggests that EPA and antioxidants in an oral supplement does not influence tumor growth in patients with cancer cachexia.

Preliminary evidence of activity from a phase II trial of doce- taxel/fristoeucean (D/F) combination in patients (pts) with ad- vanced pancreatic cancer (PC)

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D and I are among novel agents with activity in PC. Combina- tion D/F is attractive because of preclinical evidence of synergy, non-overlapping toxicities and differing mechanisms of action targeting cells in different phases of the cell cycle. Recommended phase II doses are D 35mg/m2 and I 50mg/m2 on days 1, 8, 15, and 21 of a 35 day cycle. We have enrolled 18 pts with metastatic adenocarcinoma of the pancreas on a phase II trial of this regimen. Pts had ECOG performance status 0 or 1, bidimensional measurable disease, ANC > 1500/μl, normal bilirubin, AST < 3 X upper limit of normal (ULN), alkaline phosphatase < 2.5 X ULN, and gave written informed consent. None had received prior chemotherapy. D 35 mg/m2 was infused over 1 hour, followed by 150mg/m2 over 30 minutes. Mean age was 59 (38 to 73). Principal grade 3/4 toxicities were diarrhea, neutropenia and hyperglycemia. There were 2 early deaths: 1 pulmonary embolus and 1 sudden death. Two pts have not yet undergone reevaluation. Of 14 evaluable patients, 5 (36%) achieved partial response, 5 (36%) had stable disease and 4 (28%) progressed by first reassessment. Median time on study for the 11 pts who have been removed (10 for progression, 1 for toxicity) is 5 months (m) (1 to 10.7m). Five pts remain on study at 0, 2, 8, 9 and 11m. The median survival is 8m (1 to 24m) with 7 pts alive at 0, 2, 9, 10, 11, 13, and 18m. According to our 2-stage design, there is sufficient activity to expand accrual to 37 pts.