

Canc. Gen

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METABOLISM OF BENZO[a]PYRENE (BP), N-NITROSODIMETHYLAMINE (DMN) AND N-NITROSOPYRROLIDINE (NPy) AND IDENTIFICATION OF THE MAJOR CARCINOGEN-DNA ADDUCTS FORMED IN CULTURED HUMAN ESOPHAGUS. C. C. Harris, H. Autrup, B. F. Trump and A. M. Jeffrey. Human Tissue Studies Section, LEXP, NCI, Bethesda, MD 20014, Dept. Pathology, Univ. MD., Baltimore, MD 21201 and Inst. Cancer Res., Columbia Univ., New York, NY 10032.

The 300-fold variation in the worldwide incidence of esophageal carcinoma suggests that environmental agents, including chemicals, cause this cancer. Since the interaction between chemical procarcinogens and human esophagus has not been previously studied, we examined the metabolic fate of BP, DMN and NPy in cultured non-tumorous esophagus from 2 patients with and 6 without esophageal carcinoma. Esophageal explants were cultured in a chemically-defined medium for 7 days prior to adding [3 H]BP (1.5 μ M), [14 C]DMN (100 μ M) or [14 C]NPy (100 μ M) for 24 hrs. Radioactivity was found bound to protein (BP, DMN, NPy) and to DNA (BP, DMN). The major carcinogen-DNA adducts were: 1) trans addition of BP diol epoxide I at the 10 position to the 2-amino of guanine; and 2) with DMN, N-7 methylguanine and O-6 methylguanine (O-6 MeG/N-7 MeG=0.3). The inter-individual variations in binding levels to DNA were 65-fold for BP and 10-fold for DMN. In the 2 cases studied the variation in binding levels among the 3 major anatomical segments (proximal, mid, caudal) was less than 2-fold. The metabolism of BP into water-soluble metabolites varied among the 8 patients from 1 to 68% of the total metabolism. The qualitative chromatographic patterns of water-soluble metabolites (sulphate ester (range, 21-55%), glucuronide conjugates (7-37%) and glutathione conjugates (24-66%)) and of organic-extractable metabolites were similar in all patients. Whether or not quantitative differences in carcinogen metabolism and in carcinogen bound to DNA will play a role in human susceptibility to environmental chemical carcinogens is not as yet known.

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A SENSITIVE ASSAY FOR CARCINOGEN-INDUCED EARLY CHANGES IN tRNA METHYLTRANSFERASE ACTIVITY. Elsie Wainfan, Howard Brody, and M. Earl Balis. The New York Blood Center and Memorial Sloan-Kettering Cancer Center, New York, N.Y. 10021.

Liver tRNA methyltransferases from Wistar rats treated with either acetylaminofluorene (AAF) or ethionine have been assayed using amino acid specific tRNAs from *E. coli* as substrates. When 0.06% AAF was added to the diet of male rats, which develop liver tumors after about 6 months of such treatment, selective changes in specificities of liver tRNA methyltransferases could be seen after 7 days. The maximum methyl group transfer to certain tRNAs such as tRNA^{met}, tRNA^{tyr}, and tRNA^{glu}, catalyzed by liver enzymes from treated animals was significantly higher than that seen with liver enzymes from male control rats, while transfer to tRNA^{phe}, non-initiator tRNA^{met}, and tRNA^{val} were substantially the same with enzymes from either group. Similarly, when 0.5% D,L-ethionine was fed to female rats, which develop hepatocarcinoma after about a year of ethionine ingestion, selective increases in the ability of liver enzymes to catalyze methyl group transfer to several amino acid specific tRNAs including tRNA^{met} were observed after only one week of treatment with this hepatocarcinogen. While additional changes in the activities of these enzymes occurred when the tumors developed, most of the early changes persisted. It thus appears that some characteristic pre-neoplastic alterations in tRNA methylase activities can be identified quite early in carcinogenesis. These may prove to be useful indicators of exposure to tumorigenic agents. Supported in part by NIH grants HL09011 and CA08748.

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IN VITRO BINDING OF DIETHYLNITROSAMINE (DEN) AND N-NITROSOPIPERIDINE (NPIP) TO DNA. David Y. Lai, Joseph C. Arcos and Mary F. Argus. USPHS Res. Lab., Tulane Med. Ctr., 210 State St., New Orleans, LA 70118.

Factors influencing the binding of alkylating segments from two potent carcinogenic nitrosamines to DNA were studied using an *in vitro* system containing rat liver microsomes. 14 C-DEN and 14 C-NPIP, a higher dialkyl and cyclic nitrosamine, respectively, bind to calf thymus DNA (at 37° for 1 hr). The reaction is NADPH-dependent. Pretreatment of rats with phenobarbital (PB) enhances the binding of both DEN and NPIP; binding of DEN is decreased by 3-methylcholanthrene pretreatment. The PB effect, as observed with DEN, is more pronounced with young (120-180 g) than with older (235-280 g) rats. Addition of cytosol enhances the binding of DEN 3-4 fold and that of NPIP 2-3 fold. Mitochondria increase slightly the binding of DEN and over 5-fold that of NPIP. Benzylamine (1 mM), a substrate of monoamine oxidase, inhibits the mitochondrial effect of NPIP binding by 39% and 45% in the control and PB-pretreated systems, respectively. The mitochondrial effect decreases with the decrease of nitrosamine molecular weight; mitochondria do not increase the binding of 14 C-dimethylnitrosamine to DNA.

Supported by Grant No. 922A from The Council for Tobacco Research.

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ROLE OF THE NUCLEAR PROTEIN MATRIX (NPM) IN GRANULOCYTE PYKNOSIS AND SEGMENTATION. C.E. Eastment, R.B. Scott, K.R. Shelton, J. Esar. Departments of Medicine, Pathology, Biochemistry, and Anatomy and the Cancer Center, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia 23298.

The NPM is a network of several fibrillar proteins which remains after removal of the majority of nuclear DNA, RNA, lipid and protein. Changes in this meshwork may be associated with nuclear pyknosis and segmentation occurring during granulocyte maturation. Nuclei were extracted from rabbit granulocyte precursors separated into differing stages of development in Ficoll/Hypaque density gradients, and the NPM isolated by extraction with 0.5 M NaCl followed by DNAase treatment in the presence of 8-mercaptoethanol and the protease inhibitors. NPM comprises only 10-15% of the total nuclear protein in both immature and mature granulocytes and electrophoresis on NPM in SDS-polyacrylamide gels shows that most of the protein is accounted for by a limited number of major peptides. Synthesis of NPM occurs predominantly in young precursors as shown by 35 S-methionine incorporation *in vitro*. A major difference in mature nuclei is the presence of NPM-bound DNA which is highly resistant to removal by DNAase. Scanning electron micrographs (EM) reveal intact spherical or segmented "nuclear" shapes in the NPM preparations and transmission EM show a fibrillar internal structure that is similar in both immature and mature cell nuclei. These data lead to a model of nuclear pyknosis which involves synthesis of NPM at early stages of cell development, followed by increasingly tight nuclease-resistant packing of DNA to the fibrillar NPM structure, and subsequent "collapse" of the NPM-DNA structure.

6202

PATHOLOGY

L-ETHIONINE METABOLISM IN LIVER OF RATS FED DL-ETHIONINE AND OTHER HEPATOTOXINS. Z. Brada and S. Bulba.* Papanicolaou Cancer Res. Inst., Miami, FL 33101.

The metabolism of L-ethionine (L-E) administered intraperitoneally was investigated in the liver of rats maintained for varying lengths of time on a diet containing 0.3% DL-E or 0.03% 2-N-Fluorenylacetic acid (FAA) or 0.1% 6-naphthyl isothiocyanate (NITC). Rats fasted for 16 hrs. received 100 mg/100 g body wt. (14 C) L-E and 4 hrs. later the concentration of S-adenosylmethionine (SAE) was determined. All hepatotoxins were found to decrease the accumulation of SAE in liver as follows: FAA > DL-E > NITC. SAE accumulation decreased within one week of feeding and thereafter its levels remained low for the period of observation. Except SAE, the concentration of E and its metabolites increased in the experimental rats. In comparison with the control values, the levels of E and E sulfoxide increased approximately 2 and 1.5 fold respectively in livers of rats fed DL-E for 42 days. DL-E fed rats had lower ATP concentration which did not change by L-E injection. Accumulation of SAE in liver was restored quickly after the diets containing NITC or DL-E were replaced by basal diet. In FAA-fed rats the SAE concentration also increased but it did not reach the levels found in controls. The role of methionine adenosyltransferase in the formation of SAE during these metabolic perturbations is being investigated. (Supported by USPHS Grant CA 23516.)

6204

PATHOLOGY

INCREASED ACTIVATION OF PROCARCINOGENS AFTER ETHANOL. H.K. Seitz*, A.J. Garro* and C.S. Lieber. Alcohol Research Center, V.A. Hosp., Bronx, N.Y. and Mt. Sinai Sch. of Med. (CUNY), N.Y., N.Y.

Alcoholics have an enhanced incidence of cancer of the alimentary tract and the liver. Since a variety of procarcinogens are activated through microsomal enzyme activity we wondered whether alcohol (which increases these activities) may promote the activation of procarcinogens. To study this, rats were pair fed liquid diets containing 36% of total calories as either ethanol or carbohydrates for 4 weeks. Microsomes from liver and small intestine were prepared. After alcohol feeding the activity of benzo(a)pyrene (BP) hydroxylase was significantly increased in both liver (128.7 vs. 90.5 pmoles 3-OHBP/mg microsomal protein/min; $p < 0.01$) and intestine (18.3 vs. 7.1; $p < 0.01$). We also found that the capacity of hepatic and intestinal microsomes to activate BP to a mutagen for *Salmonella typhimurium* TA 100 was significantly increased. Furthermore activation of 2-aminofluorene and tryptophan pyrrolizate to mutagens by intestinal microsomes was significantly enhanced. Moreover, there was an increased activity of hepatic demethylation of dimethylnitrosamine, a known procarcinogen (1.81 $\pm$ 0.12 vs. 1.14 $\pm$ 0.08 nmoles formaldehyde/mg microsomal protein/min; $p < 0.01$). In conclusion, chronic ethanol ingestion increases the activation of procarcinogens in liver and intestine; this may contribute to the enhanced incidence of various cancers in the alcoholic. (Supported by the VA, NIAAA and NIAID).

6206

PATHOLOGY

CORRELATION BETWEEN IRON-INDUCED LIPOPEROXIDATION AND "UN-SCHEDULED" DNA SYNTHESIS IN ISOLATED NUCLEI AND CULTURED HEPATOCYTES. Thomas K. Shires and Charles Lovig*. Department of Pharmacology, University of Iowa, Iowa City IA 52242

In freshly isolated rat liver nuclei, the stimulation of lipoperoxidation (LPO - measured by thiobarbituric acid assay for malondialdehyde) by Fe^{3+} was accompanied by incorporation of 3H -dTTP into DNA as demonstrated by acid precipitation or in $CaCl_2$ - $CaSO_4$ gradients. Incorporation was dependent on the combined presence of dGTP, dATP, dTTP and dCTP but did not require ATP and was insensitive to hydroxyurea. Neither LPO nor incorporation occurred at $< 1 \mu M$ or $> 25 \mu M$ Fe^{3+} per $4 OD_{280}$ units of nuclei, while both were maximal at $10 \mu M$. Incorporation as well as LPO was inhibited by α -tocopherol, superoxide dismutase, catalase, hydroxybutyltoluene, or mannitol. LPO produced by NADPH or by ascorbic acid also correlated with 3H -dTTP incorporation. As little as 1 mMole of pure malondialdehyde incubated with $4 OD_{280}$ nuclei also stimulated 3H -dTTP incorporation. Preliminary studies with non-proliferating rat hepatocytes cultured on collagen substrate indicate that Fe^{3+} stimulates 3H -dTTP incorporation into DNA at concentrations less than those that depress viability (measured by dye uptake) below 90%. The involvement of lipoperoxidation in the mechanism of iron-related carcinogenesis is considered. (Supported in part by USPHS NIH Grant 12675.)

6203

PATHOLOGY

REPAIR OF ULTRAVIOLET RADIATION- AND N-ACETOXY-2-ACETYLAMINO-FLUORENE-INDUCED DNA DAMAGE IN PERMEABILIZED HUMAN CELLS. John D. Roberts* and Michael W. Lieberman. Washington University School of Medicine, St. Louis, Missouri 63110

We have developed a system for studying DNA repair synthesis in permeabilized, human diploid fibroblasts. With a synthesis mixture containing dATP, dGTP, dTTP and ^{32}P -labeled dCTP, the incorporation of labeled nucleotides into parental DNA ($\rho = 1.73 \text{ g/cm}^3$ in alkaline $CaCl_2$) was stimulated 10-20 fold by the exposure of the cells to either UV or N-acetoxy-2-acetylaminofluorene; this damage-dependent DNA synthesis was absent when cells deficient in excision repair (xeroderma pigmentosum, complementation group A) were used. Repair synthesis in this system was strongly dependent upon ATP and Mg^{2+} , had a pH optimum in Tris/HCl of 8.0, was inhibited by NaCl, and was only partially dependent upon the addition of exogenous dNTPs. The reaction was linear for 10 minutes and continued for at least one hour. Labeled deoxycytidine and dCMP were also incorporated during repair synthesis but at reduced levels (38% and 88%, respectively) when compared to dCTP. The addition of β -NAD $^{+}$ (the active form of the co-factor), α -NAD $^{+}$ (a competitive inhibitor), or nicotinamide had little effect on repair synthesis in this system. This permeabilized cell system should be useful in the further characterization of the molecular events involved in eukaryotic DNA repair. (Supported in part by NIH Grant CA 20513.)

6205

PATHOLOGY

HEPATIC RNA SYNTHESIS IN RATS TREATED WITH ETHYLENE THIOUREA. Garth E. Austin and Geoffrey M. Moyer. UCLA Pathology Dept., Los Angeles, Ca. 90024.

Ethylene thiourea (ETU) is the major degradation product of the ethylene-bis-dithiocarbamate fungicides which are used on agricultural crops. This compound has been reported to produce tumors of thyroid and liver after prolonged administration to rats or mice. However, *in vitro* testing has indicated that the compound is not mutagenic, suggesting that ETU may not be an initiator of carcinogenesis. Another property we have found to be common to most and possibly all carcinogens is the ability to inhibit transcription. Thus, we have examined the effect of ETU administration on RNA synthesis in rat liver. The compound was administered to rats by intraperitoneal injection, by nasogastric tube or in the diet. Even doses which produced extreme clinical toxicity and marked depression of serum thyroxine levels brought about no reduction in the rate of nuclear or cytoplasmic RNA synthesis. By contrast, the structurally related weak hepatocarcinogen, thioacetamide, at comparable doses, did inhibit liver RNA synthesis as did the potent hepatocarcinogen, N-2 acetylaminofluorene. These results support the suggestion that ETU is not a direct-acting carcinogen but that it increases tumor incidence by an indirect mechanism, possibly involving its antithyroid properties. (Supported by a gift from Rohm and Haas, Philadelphia, Pa.)

6207

PATHOLOGY

LONG TERM MAINTENANCE OF NORMAL HUMAN ENDOMETRIAL CELLS IN MONOLAYER CULTURE. T.A. Adamec*, S.A. Melin*, and D.G. Kaufman. Department of Pathology, University of North Carolina, Chapel Hill, NC 27514

In an effort to better understand the process of carcinogenesis in human endometrial tissue, methods have been developed for the prolonged maintenance of this tissue in monolayer cultures. Endometrial tissue was obtained from hysterectomy specimens of consenting patients with no evidence of intrinsic endometrial disease. Endometrium was enzymatically dispersed into single cells and plated at high density; cultures were obtained from all specimens. Five morphologic types of cells were observed including two presumed to be immature and mature epithelial cells. All types except the presumed mature epithelial cells were readily subcultured. Treatment of presumed immature epithelial cells with 17 β -estradiol followed by 17 β -estradiol plus progesterone caused rearrangement of cells into gland-like clusters with PAS-positive cytoplasmic material. This response was retained after multiple passages or storage of cells in liquid nitrogen. Fibroblasts treated similarly did not respond, nor did epithelial cells not primed with 17 β -estradiol. These results show a greater rate of establishment of long-term human endometrial cell cultures and a more normal response to hormones than in previous reports. (Supported by NCI contract CP75956 and grants CA00431 and CA17973)

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SHORT-TERM IN VIVO MAMMALIAN PRE-SCREEN FOR PULMONARY CARCINOGENS

F. BOJAN, P. RADY, I. ARANY, É. UZVÜLGYI and P. KERAI
/Dept. Hyg. Epid., Med. Univ. School, Debrecen, Hungary/

The activities of pyruvate kinase /PK/ and lactate dehyd-
rogenase /LDH/ as well as the isozymic pattern of LDH in
lungs of C57BL mice treated with a variety of carcinogens
and non-carcinogens were determined 28 days after the single
exposure to the chemicals.

In the lungs of adult mice treated with the potent carci-
nogens urethane, dimethylnitrosamine, 2-methylcholanthrene,
benzo/a/pyrene, 7,12-dimethylbenz/a/anthracene and aflatoxin
B₁ the activities of PK and LDH increased and the isozymic
pattern of LDH shifted towards the tumorous pattern. However,
exposure to the non-carcinogenic analogues phenylurethane,
ethylformate, chrysene, perylene and pyrene as well as the
non-carcinogenic pulmonary toxicants Paraquat, butylated
hydroxytoluene and cadmium chloride caused no alterations
in the enzyme activities. Transplacental exposure to the
carcinogens also resulted enzyme alterations very similar
to those observed in adult mice.

According to the results it can be supposed that the car-
cinogenicity of chemicals might be predicted by the determi-
nation of activities of PK and LDH in mouse lung even before
the macroscopic appearance of lung tumors.

INDUCTION OF LIVER ALDEHYDE DEHYDROGENASE ACTIVITY - AN INDICATOR OF CHEMICAL EXPOSURE?

R. TÖRRÖNEN, H. NOUTAINEN and M. MARSELOS (Department of Physiology,
University of Kuopio, Kuopio, Finland)

The cytosolic aldehyde dehydrogenase activity of rat liver is increased due to
exposure to several foreign chemicals. The best-known example is the induction
by phenobarbital. In the Wistar rat the response to phenobarbital is deter-
mined by genetic factors. A similar, genetically determined induction was
observed also after the administration of p,p'-DDT.

Another type of induction of the hepatic aldehyde dehydrogenase activity is
produced by TCDD, 3,4-benzopyrene and 3-methylcholanthrene. The induction by
these toxic agents is not under the same genetic control as the induction by
phenobarbital. A new isoenzyme is formed and it can be differentiated from the
normal and phenobarbital-inducible isoenzymes in a simple way: it is active with
benzaldehyde as a substrate and NADP as a coenzyme, whereas the other enzymes
are not. A 40-fold induction of the hepatic aldehyde dehydrogenase activity was
observed after the administration of a single dose (80 µg/kg) of TCDD. The
highly carcinogenic polycyclic hydrocarbons 3,4-benzopyrene and 3-methylcholan-
threne (100 mg/kg daily for 4 days) produced a 30-fold increase and the weakly
carcinogenic 1,2-benzanthracene a 9-fold increase in the activity. On the
contrary, administration of the non-carcinogenic polycyclic hydrocarbons anthra-
cene, phenanthrene and chrysene produced only a 2-3-fold induction. Thus in
this group of six polycyclic hydrocarbons there seems to be a correlation
between the carcinogenicity of the compound and the induction of the hepatic
aldehyde dehydrogenase activity. No induction, however, was observed with a
similar dose of the carcinogenic 2-acetylaminofluorene or urethane.

can be studied in specific organs of Chinese hamsters after acute dosing with chemical carcinogens.

In preliminary experiments an increase in mutation at both loci was detected in cultures derived from lung tissue of 3-week-old Chinese hamsters after intraperitoneal dosing with ethyl methanesulphonate or diethylnitrosamine. Subsequent experiments have shown the induction of mutation in cells derived from the bladder of animals dosed with diethylnitrosamine or methyl nitrosourea, and in a variety of other tissues from animals dosed with methanesulphonates, 2-acetylaminofluorene and urethane.

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Pool, B.L., German Cancer Research Center, Institute for Toxicology and Chemotherapy, Im Neuenheimer Feld 280, 6900 Heidelberg (West-Germany)

Comparison of synergism in mutagenesis and carcinogenesis assays

Combination effects of chemical carcinogens were investigated in the Ames test system under a variety of conditions. The studies were performed in order to establish a new parameter for correlation of mutagenesis and carcinogenesis. It was also performed in order to gain knowledge on potential synergism of compounds, since man is exposed to a complex of different types of chemicals. An attempt was made to answer the following questions: 1. Are synmutagenic effects present under the described experimental conditions? 2. How do combination effects in the mutagenesis assay compare to those from long-term carcinogenicity experiments?

Four pairs of test compounds were chosen for the investigations: (a) benzo(a)pyrene and diethylnitrosamine; (b) 4-dimethylamino-azobenzene and diethylnitrosamine; (c) 4-dimethylaminostilbene and diethylnitrosamine; (d) urethane and 7,12-dimethylbenzanthracene. The first two pairs of compounds indicated the presence of additive effects whereas the latter two did not. These results would correlate to those of long-term carcinogenicity experiments in vivo, which had a similar outcome. The validity of these results and the possibilities of using the Ames assay for studying synergistic effects of compounds will be discussed.

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Hartley-Asp, B., AB Leo, Research Laboratories, 251 00 Helsingborg (Sweden)

Metronidazole: chromosome analysis in patients treated for *Trichomoniasis vaginalis*, and the micro-nucleus test in mice

Metronidazole (Flagyl®) and its analogs have exhibited mutagenic activity in *Salmonella*, *Klebsiella pneumoniae* and *Citrobacter freundii* in the plate test and the fluctuation assay. However, little information is available from higher organisms. Therefore we carried out cytogenetic studies in mammalian and human cells in vitro and in vivo. Human lymphocytes were exposed to doses

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Proc. Am. Ass. Cancer Res.
74 7-and

Abstracts, 1973

- 25 MEGALOCYTE INDUCTION IN LIVERS OF RATS TREATED WITH METHYLAZOXYMETHANOL ACETATE. M. S. Zedeck, S. S. Sternberg and J. McGowan. Sloan-Kettering Institute for Cancer Research, New York, N. Y. 10021

Methylazoxymethanol acetate (MAMac), a hepatocarcinogen, induces within hours a number of diverse biochemical and pathological changes in rat liver. To determine whether other changes are initiated but not immediately evident rats were partially hepatectomized 1 wk after a single injection of MAMac (35 mg/kg). At 48 hr after partial hepatectomy (HEPX) more than 90% of hepatocytes were enlarged indicating that almost all parenchymal cells had been altered by MAMac. At 96 hr abnormal mitoses were present. By 7 days only 35% of the cells were megalocytes. HEPX as late as 8 wk after treatment with MAMac induced megalocytosis indicating the long persistence of the latent effect. Similar treatment with the non-hepatocarcinogen actinomycin D which like MAMac causes early changes in nucleolar structure and in RNA synthesis did not result in the formation of megalocytes. Preliminary experiments indicate that HEPX 1 wk after MAMac does not increase the incidence of animals with hyperplastic foci and hepatocellular carcinoma. (Supported, in part, by NCI Grant CA 08748.)

- 26 INHIBITION OF CHEMICAL CARCINOGENESIS BY BUTYLATED HYDROXYANISOLE (BHA) AND THIURAM DISULFIDE DERIVATIVES. Lee W. Wattenberg. Department of Pathology, University of Minnesota, Minneapolis, MN 55455.

BHA inhibits carcinogenic effects of 7,12-dimethylbenz(a)anthracene (DMBA) and benzo(a)pyrene (BP) on mouse forestomach and diethylnitrosamine and 4-nitroquinoline-N-oxide on mouse lung (J. Nat. Canc. Inst. 48, 1425, (1972); Fed. Proc. 31, 633, (1972)). Further inhibitory effects of BHA are reported now as well as studies with thiuram disulfide antioxidants. Groups of female A/HeJ mice were placed on diets with or without BHA 5 mg/g. They were then given BP 3 mg or DMBA 0.75 mg X 2 doses per os at 14 day intervals, uracil mustard 0.05 mg X 4 doses per os over 14 days or urethane 10 mg i.p.. In about 20 weeks average number of pulmonary adenomas per mouse were (groups designated by carcinogen and diet; control, C or BHA): BP-C 5.3 - BP-BHA, 2.5; DMBA-C 28.2 - DMBA-BHA, 12.7; uracil mustard-C 9.3 - uracil mustard - BHA, 3.8 and urethane-C 12.3 - urethane-BHA, 2.7. Female Ha/ICR mice were fed diets containing BP 0.3 mg/g with or without tetraethylthiuram disulfide (TETD) 10mg/g or tetrabutylthiuram disulfide (TBTD) 10mg/g for 6 weeks. 14 weeks later the average number of tumors of forestomach per mouse were: no antioxidant, 3.7; TETD, 0.4; and TBTD, 0.9. TETD and TBTD inhibit DMBA induced (30mg per os) adrenal necrosis in rats. Data show a considerable diversity of inhibitory effects of antioxidants against chemical carcinogens.

- 27 MALIGNANT TRANSFORMATION IN VITRO OF MOUSE FIBROBLASTS BY 7,12-DIMETHYLBENZ(A)-ANTHRACENE, 7-HYDROXYMETHYLBENZ(A)ANTHRACENE AND BY THEIR 'K-REGION' DERIVATIVES. H. Marquardt, J. E. Sodergren, P. Sims, and P. L. Grover. Sloan-Kettering Inst., New York, N.Y. 10021 and Chester Beatty Res. Institute, London, UK.

'K-region' epoxides of benz(a)anthracene, dibenz(a,h)anthracene and 3-methylcholanthrene are more active in producing malignant transformation of cells in culture than the parent hydrocarbons and may be "proximate carcinogens". Transformation by these parent hydrocarbons is influenced by alterations in the activity of microsomal mixed-function oxidases. However, similar alterations do not modify transformation by 7,12-dimethylbenz(a)anthracene.

We now report on transformation experiments where fibroblasts derived from C3H mouse prostate were treated with the K-region epoxides of 7,12-dimethylbenz(a)anthracene and of 7-hydroxymethylbenz(a)anthracene that are known microsomal metabolites of these hydrocarbons. The epoxides were more lethal but they produced fewer transformed foci than the parent hydrocarbons. Neither the toxic 'K-region' phenols nor the corresponding non-toxic *cis*-dihydrodiols induced transformation.

These and other data indicate that in 7-methyl-substituted benz(a)anthracenes transforming activity and stability of 'K-region' epoxides are decreased. The involvement of epoxides in carcinogenesis by these hydrocarbons remains unproven. (Supported in part by Grant CA 08748 from the National Cancer Inst.)

- 28 ANALYSIS OF ¹²⁵I-LABELED ANTIGLIOMA ANTIBODIES ADSORBED BY INTACT MONOLAYERS OF CULTURED GLIOMA CELLS. Eugene D. Day and Darell D. Bigner. Duke University Medical Center, Durham, N. C. 27710.

The sequential method of adsorption analysis (J. Immunol. 107:1611, 1971) was applied to anti-glioma radioantibodies adsorbed by intact monolayer cultures of glioma cells. A non-centrifugal technique was devised to permit transfer of radioantibody solutions from one culture to the next in a sequence, and to effect removal of unbound radioglobulins. When established mycoplasma-free clonal lines of the N-nitrosomethylurea-induced C6 rat astrocytoma and 2 different rat fibroblast cultures were utilized, simple primary binding of ¹²⁵I-IgG was readily measured in a particularly sensitive and reproducible manner over and above control IgG. With proportions varying from one serum to the next, all anti-glioma radioantibodies from 9 different rabbit antisera, after preadsorption x 3 with rat liver, still retained cross-reactivity for fibroblast cultures, and, after adsorption x 3 with fibroblasts, still retained selective reactivity for glioma cells. When adsorbed with glioma cells first, the bulk of all binding activity remained with the glial cells. When varying amounts of unlabeled antibody IgG were mixed with fixed quantities of labeled antibody IgG and glioma cells, an equivalence point was established by competitive binding curves and, independently, by microscopic examination of the monolayer-antibody complexes after light trypsinization: cell clumps in excess antibody; free cells otherwise. Parameters of IgG binding could be obtained; e.g., $K = 2 \times 10^6 M^{-1}$, $a = 0.66$, and $s = 6.7 \times 10^7$ sites/cell.

NINDS-NS-10237 and NCI-CA-11898

- 94 AU - GRAF W
 TI - Danger of carcinogenic substances in the environment.
 SI - HEEP/72/01988
 SO - OEFF GESUNDHEITSWES; 33 (3). 1971 121-133
 AB - HEEP COPYRIGHT: BIOL ABS. Despite an alarmingly large number of known chemical, physical and biological carcinogenic substances, there is still no satisfactory explanation of the etiology of carcinoma development. Aside from this, 3/4 of all types of cancer are attributed to exogenous environmental factors. The Druckrey summation theory is valuable for judging the overall carcinogenic situation. Only a dosage-related study of the toxicology of these damaging substances promises any progress. With regard to the dangers of exposure for modern man, the essential distinction must be made between occupational, environmental and natural cancer hazards. Among the natural carcinogenic substances, nitrosamine, mycotoxins (aflatoxin) and 3,4-benzpyrene and its derivatives play a decisive role.
- 95 AU - DI PAOLO JA ; DONOVAN PJ ; NELSON RL
 TI - TRANSFORMATION OF SYRIAN HAMSTER FETAL CELLS IN-VITRO BY CHEMICAL CARCINOGENS
 SI - HEEP/72/00856
 SO - PROC AMER ASS CANCER RES; 12. 1971 65
 AB - HEEP COPYRIGHT: BIOL ABS. ABSTRACT X IRRADIATION BENZO-A-PYRENE 2 ACETYL AMINO FLUORENE AFLA TOXIN B-1 DI BENZ ANTHRACENE 1 METHYL CYCLO PENTA-OL PHENATHREN-17-ONE 3 HYDROXY BENZO-A-PYRENE 7 12 DI METHYL BENZ-A ANTHRACENE URETHANE N HYDROXY URETHANE DI ETHYL NITROSAMINE
- 96 AU - Sula JP
 AD - Med. Fac., Charles Univ., Prague, Czech.
 TI - Nature, precursor of civilization in chemical carcinogenesis
 SI - CA/079/074373B
 SO - Prot. Vitae; VOL 17, ISS 6, 1972,215-8
 LA - Ger
 AB - CBAC COPYRIGHT: CHEM ABS A review with 30 refs. on the occurrence of carcinogens such as 3,4-benzpyrene (I), dimethylnitrosamine, ethionine, aflatoxin, sterigmatocystine, and luteoskyrine, in the environment and their potential in producing tumors. (50-32-8 3,4-Benzpyrene)(62-75-9 Dimethylnitrosamine)(13073-35-3 Ethionine)(1402-68-2 Aflatoxin)
- 97 AU - Kolesnichenko TS
 AD - Inst. Exp. Clin. Oncol., Moscow, USSR
 TI - Transplacental action of some carcinogens in organ cultures of golden hamster embryonal pulmonary tissues
 SI - CA/078/106794N
 SO - Vop. Onkol.; VOL 18, ISS 10, 1972,48-52
 LA - Russ
 AB - CBAC COPYRIGHT: CHEM ABS Proliferation of the bronchial epithelium of hamster embryonic pulmonary tissue explants occurred when the mother animals in the last third of pregnancy

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received 20 mg 9,10-dimethyl-1,2-benzanthracene (I), 0.02 mg diethylnitrosamine, or 6 mg nitrosomethylurea. (57-97-6 9,10-Dimethyl-1,2-benzanthracene)(55-18-5 Diethylnitrosamine)(684-93-5 Nitrosomethylurea)

- 98 AU - Schmaehl D ; Krueger C ; Preissler P
 AD - Inst. Exp. Toxikol. Chemother., Dtsch. Krebsforschungszentrum Heidelberg, Heidelberg, Ger.
 TI - Cancer prophylaxis by vitamin A
 SI - CA/077/122058K
 SO - Arzneim.-Forsch.; VOL 22, ISS 5, 1972,946-9
 LA - Ger
 AB - CBAC COPYRIGHT: CHEM ABS Oral administration of vitamin A or

from a comparison between mutagenicities with intact hepatocytes and with S9 prepared from disrupted hepatocytes. The results support previous recommendations that tests with intact cell metabolism should be included in a battery for screening of carcinogens in vitro.

- 25 AU - ANON
TI - Chimneysweeps die young
SI - CIS/82/01394
SO - Working Environment 1982, p.18-20. Illus.
LA - Eng
AB - Nearly 3 times as many chimneysweeps in Sweden die of lung cancer than would be normal; 5 times as many die of throat cancer. There were 441 deaths among the 2,495 chimneysweeps studied, compared with an expected figure of 355 (excess mortality of 24%); of these, 32 died of lung cancer, against an expected figure of 12, i.e. nearly 3 times the normal population rate. 8 chimneysweeps died of oesophageal cancer, whereas 1.6 such deaths could normally be expected (5 times the normal population rate). Liver cancer also was 5 times the normal population rate. Cardiovascular diseases killed 182 of chimneysweeps studied, against an expected figure of 152. Hazards to which chimneysweeps are exposed: polycyclic aromatic compounds (including benzo(a)pyrene), nitrogen compounds which can convert into nitrosamines), arsenic, asbestos, sulfur dioxide, carbon monoxide, solvents (for cleaning ventilation channels). Mortality among chimneysweeps could be reduced by use of respirators, expansion of
- 26 AU - J'arvholm B ; Lavenius B
TI - A cohort study on cancer among workers exposed to an antirust oil
SI - CIS/82/00801
SO - Scandinavian Journal of Work, Environment and Health Sep. 1981, Vol.7, No.3, p.179-184. 15 ref.
LA - Eng
AB - 3 groups of a total of 98 workers who had worked in a packing department between 1954 and 1957 in which an antirust oil containing N-phenyl-1-naphthylamine (PNA) and sodium nitrite (NaNO₂) was used, 33 workers in a different packing department and exposed only NaNO₂, and 31 workers who had exhibited eczema as a result of exposure to PNA in the oil, were examined for excess cancer. Among women exposed to the oil containing PNA 12 cancer cases were found versus 3.9 expected. The tumours were situated in the uterus, ovaries, breast, thyroid, brain, colon and bladder. No known carcinogenic substance was found that could explain this increased incidence but PNA, or its nitroso derivative, is likely to be the causative agent.

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- 142 AU - INOUE K ; SUHAKAWA T ; OKAMOTO K ; TANAKA Y
TI - MUTAGENICITY TESTS AND IN VITRO TRANSFORMATION ASSAYS ON
TRIETHANOLAMINE
SI - EMIC/82/004651
SO - MUTAT RES; 101:305-313,1982
LA - ENG
AB - EMIC/ORNL SEE: CA 97-86746
- 143 AU - MUH N ; NEMOTO N ; UTAKOJI T
TI - METABOLIC ACTIVATION OF BENZO(A)PYRENE, AFLATOXIN B1, AND
DIMETHYLNITROSAMINE BY A HUMAN HEPATOMA CELL LINE
SI - EMIC/82/004627
SO - MUTAT RES; 94:339-348,1982
LA - ENG
AB - EMIC/ORNL SEE: CA 97-51017
- 144 AU - ABE S ; SASAKI M
TI - INDUCTION OF SISTER-CHROMATID EXCHANGES BY INDIRECT
MUTAGENS/CARCINOGENS IN CULTURED RAT HEPATOMA AND ESOPHAGEAL
TUMOR CELLS AND IN CHINESE HAMSTER DON CELLS CO-CULTIVATED WITH
RAT CELLS
SI - EMIC/82/004253
SO - MUTAT RES; 93:409-418,1982
LA - ENG
AB - EMIC/ORNL
- 145 AU - AMACHER DE ; TURNER GN
TI - THE EFFECT OF LIVER POSTMITOCHONDRIAL FRACTION CONCENTRATION FROM
AROCLOR 1254-TREATED RATS ON PROMUTAGEN ACTIVATION IN L5178Y CELLS
SI - EMIC/82/004237
SO - MUTAT RES; 97:131-137,1982
LA - ENG
AB - EMIC/ORNL SEE: CA 96-175811
- 146 AU - CHEN DJ ; OKINAKA RT ; STRNISTE GF ; BARNHART BJ
TI - INDUCTION OF 6-THIOGUANINE-RESISTANT MUTATIONS BY RAT-LIVER
HOMOGENATE (S9)-ACTIVATED PROMUTAGENS IN HUMAN EMBRYONIC SKIN
FIBROBLASTS
SI - EMIC/82/004213
SO - MUTAT RES; 101:87-98,1982
LA - ENG
AB - EMIC/ORNL SEE: CA 96-175418
- 147 AU - PAINTER RB ; HOWARD R
TI - THE HELA DNA-SYNTHESIS INHIBITION TEST AS A RAPID SCREEN FOR
MUTAGENIC CARCINOGENS
SI - EMIC/82/004200
SO - MUTAT RES; 92:427-437,1982
LA - ENG
AB - EMIC/ORNL SEE: CA 96-175817

- 148 AU - PARODI S ; TANINGHER M ; BDERO P ; SANTI L
TI - QUANTITATIVE CORRELATIONS AMONGST ALKALINE DNA FRAGMENTATION, DNA
COVALENT BINDING, MUTAGENICITY IN THE AMES TEST AND
CARCINOGENICITY, FOR 21 COMPOUNDS
SI - EMIC/82/004142
SO - MUTAT RES; 93:1-24,1982
LA - ENG
AB - EMIC/ORNL SEE: CA 96-117313
- 149 AU - SUTER W ; JAEGER I

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- 248 AU - Feron VJ ; Kruijsse A ; Moutersen RA
AD - Institute CIVD-Toxicology and Nutrition TNO, Zeist, The Netherlands.
TI - Respiratory tract tumours in hamsters exposed to acetaldehyde vapour alone or simultaneously to benzo(a)pyrene or diethylnitrosamine.
SI - TOXBIB/82/210845
SO - Eur J Cancer Clin Oncol; VOL 18, ISS 1, 1982, P13-31
LA - Eng
- 249 AU - Ogawa K ; Yokokawa K ; Tomoyori T ; Ono'e T
AD - Department of Pathology, Sapporo Medical College, Sapporo, Japan.
TI - Induction of gamma-glutamyltranspeptidase-positive altered hepatocytic lesions by combination of transplacental-initiation and postnatal-selection.
SI - TOXBIB/82/166490
SO - Int J Cancer; VOL 29, ISS 3, 1982, P333-6
LA - Eng
- 250 AU - Pitot HC ; Goldsworthy T ; Moran S ; Sirica AE ; Weeks J
AD - McArdle Laboratory for Cancer Research, Department of Oncology Medical School, University of Wisconsin, Madison.
TI - Properties of incomplete carcinogens and promoters in hepatocarcinogenesis.
SI - TOXBIB/82/162602
SO - Carcinog Compr Surv; VOL 7, 1982, P85-98 (REF: 48)
LA - Eng
- 251 AU - BOGOVSKII PA
TI - THE DEVELOPMENT OF EXPERIMENTAL ONCOLOGY IN THE ESTONIAN-SSR USSR
SI - HEEP/84/04122
SO - EKSP ONKOL; 4 (6). 1982 (RECD. 1983). 66-67.
LA - RUS
AB - HEEP COPYRIGHT: BIOL ABS. REVIEW HUMAN BENZO A PYRENE NITROSO DI ETHYLAMINE POLY CYCLIC AROMATIC HYDRO CARBON CARCINOGEN HEPATOMA OIL REFINING POLLUTION
- 252 AU - POLAND A ; PALEN D ; GLOVER E
TI - TUMOR PROMOTION BY TETRA CHLORO DI BENZO-P-DIOXIN IN SKIN OF HRS-J HAIRLESS MICE
SI - HEEP/83/12949
SO - NATURE (LOND); 300 (5889). 1982. 271-273.
LA - ENG
AB - HEEP COPYRIGHT: BIOL ABS. DI METHYL BENZ A ANTHRACENE N METHYL-N'-NITRO-N-NITROSO GUANIDINE CARCINOGEN DIOXIN PAPILLOMA ENVIRONMENTAL TOXICANT

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- 253 AU - HAUSER TR ; BROMBERG SM
TI - ENVIRONMENTAL PROTECTION AGENCY MONITORING PROGRAM AT LOVE CANAL NEW-YORK USA 1980
SI - HEEP/83/12302
SO - ENVIRON MONIT ASSESS; 2 (3). 1982 (RECD. 1983). 249-272.
LA - ENG
AB - HEEP COPYRIGHT: BIOL ABS. INDUSTRIAL POLLUTION HAZARDOUS WASTE DISPOSAL
- 254 AU - MIRSALIS JC ; TYSON CK ; BUTTERNORTH BE

... a new Carcinogenicity test system in rats, in vivo-in vitro, is discussed in light of the validation results obtained so far. The new test lasts only 3 wk and involves the use of peritoneal cells as target cells. Colony growth in soft agar is considered as a criterion for cell transformation which, in turn, is taken as evidence for a carcinogenic potential of the agent tested. There was an absence of colony growth in 98% of the cultures made from the 225 control rats tested so far. Neg. results were also obsd. with 2 known noncarcinogens, whereas pos. cultures were obsd. for 7 known carcinogens belonging to 5 different classes. These chosen target cells are sensitive enough to detect the carcinogenic effect of agents applied in vivo even if these are strictly organotropic in their action.

129 AU - Li M
AD - Inst. Cancer Res., Chin. Acad. Med. Sci., Peking
TI - Studies on potential carcinogens in the diet of individuals at high risk for esophageal cancer
SI - CA/094/186612V
SO - Cancer Res. People's Repub. China U. S. A.: Epidemiol., Causation New Approaches Ther., (Proc. Conf; 1981,131-6
LA - ENG

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AB - CBAC COPYRIGHT: CHEM ABS The formation of DMN, diethylnitrosamine, methylbenzyl nitrosamine, and N-(1-methylacetyl)-N-(3-methylbutyl) nitrosamine was demonstrated in moldy cornbread after an 8-day incubation following the addn. of NaNO₂. (62-75-9 DMN)(55-18-5 Diethylnitrosamine)(937-40-6 Methylbenzyl nitrosamine)(71016-15-4 N-(1-methylacetyl)-N-(3-methylbutyl) nitrosamine) Cornbread inoculated with *Fusarium moniliforme* and treated with NaNO₂ caused tumors in rats. Roussin red Me ester was isolated from pickled vegetables and this compd. induced forestomach tumors in mice. (16071-96-8 Roussin red methyl ester) Benzo[a]pyrene (I) and other polycyclic arom. hydrocarbons were isolated from the pickled vegetables. (50-32-8 Benzo[a]pyrene) The results were discussed in relation to the diet of individuals at high risk for esophageal cancer.

130 AU - Okinaka RT ; Barnhart BJ ; Chen DJ
AD - Los Alamos Sci. Lab., Univ. California, Los Alamos
TI - Comparison between sister-chromatid exchange and mutagenicity following exogenous metabolic activation of promutagens
SI - CA/094/059300S
SO - Mutat. Res.; VOL 91, ISS 1, 1981,57-61
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Benzo[a]pyrene (I) and dimethylnitrosamine (DMN) were toxic to Chinese hamster ovary (CHO) cells after being metabolically activated with S9 proteins. (50-32-8 Benzo[a]pyrene)(62-75-9 Dimethylnitrosamine) In contrast, neither compd. elicited a cytotoxic effect when microsomal enzymes were not present. At 1-4 mug/mL, I and DMN induced mutation and sister chromatid exchange (SCE) in the presence of S9 protein. The response, as a function of dose, was pos. and linear. A pos. relation apparently exists between mutation and SCE when an exogenous supply of rat liver microsomes is used to activate the promutagens, and SCE anal. may therefore be a useful measure of genetic damage in systems utilizing metabolic activation.

131 AU - Pesch GG ; Pesch CE ; Malcolm AR
AD - Environmental Research Lab., Narragansett, RI.
TI - 'Neanthes arenaceodentata', a Cytogenetic Model for Marine Genetic Toxicology
SI - NTIS/PB82-169202
SO - Govt Reports Announcements & Index (GRA&I), Issue 12, 1982
OD - NTIS/PB82-169202, 13p
PR - NTIS Prices: PC A02/MF A01
AB - ID3: Genetic toxicants are present in polluted marine environments and may represent a long-term threat to populations of marine organisms. A cytogenetic model is useful to study the effects of these toxicants. The polychaeta, *Neanthes arenaceodentata*, was chosen as such model because it has a

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(SCE) analysis, a sensitive cytogenetic technique, to this marine worm. In earlier studies, *N. arenaceodentata* exhibited a dose response to mitomycin C (MMC) at concentrations comparable to those that elicited responses in in vivo mammalian systems. Exposure to 5 times 10 to the 7th power M MMC for 48 h increased the frequency of SCE in the worm from a baseline value of 0.14 exchanges/chromosome to 0.5 exchanges/chromosome. Positive SCE responses in the worm have also been demonstrated in this study for other known, direct-acting mutagens such as 5-bromodeoxyuridine and methylmethanesulfonate, as well as for compounds that need metabolic activation such as benzo(a)pyrene, dimethylnitrosamine and cyclophosphamide. These results imply that *N. arenaceodentata* can metabolize promutagens and suggest that the worm may be sensitive to a broad spectrum of genetic toxicants. The significance of these findings, as well as directions for future research, are discussed. Journal article

132. AU - Baines TM
AD - Environmental Protection Agency, Ann Arbor, MI. Control Technology Assessment and Characterization Branch.
TI - Nitrosamines and Other Hazardous Emissions from Engine Crankcases
SI - NTIS/PB82-127960
SO - Govt Reports Announcements & Index (GRA&I), Issue 06, 1982
OO - NTIS/PB82-127960, 15p
PR - NTIS Prices: PC A02/MF A01
AB - TD3: The emissions from heavy duty Diesel crankcases contain a number of hazardous compounds. Research has discovered some of them and it may be possible that there are some that have not yet been quantified. Nitrosamines (a potent carcinogen in animals and probably also in humans) are emitted from engines using fresh oil. These emissions seem to be a function of the type of oil used and some engine parameters such as crankcase flow rate of NOx compounds. Used lubricating oil has been shown to contain carcinogenic compounds such as benzo-a-pyrene. It has also been shown to be mutagenic. Therefore it can be concluded that the particulate portion of the crankcase effluent stream may start out after an oil change at a level containing few carcinogenic compounds but the level of these compounds increases with time. In conclusion, crankcases emit a variety of hazardous chemicals and evaluation of the costs and benefits of the control of these emissions should be seriously considered. Technical rept.
133. AU - Langenbach R ; Malick L ; Nesnow S
AD - Health Effects Research Lab., Research Triangle Park, NC.
TI - Rat Bladder Cell-Mediated Mutagenesis of Chinese Hamster V79 Cells and Metabolism of Benzo(a)Pyrene
SI - NTIS/PB82-127382
SO - Govt Reports Announcements & Index (GRA&I), Issue 05, 1982
OO - NTIS/PB82-127382, 7p
PR - NTIS Prices: PC A02/MF A01
AB - TD3: Primary rat bladder epithelial cells were cocultivated with Chinese hamster V79 cells in the presence of carcinogens, and the induction of 6-thioguanine resistance in the V79 cells was used

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alkaline sucrose gradient centrifugation; unscheduled DNA synthesis (UDS) in CRFK, Syrian hamster embryo (SHE) and rat hepatocyte cultures measured by liquid scintillation counting; and UDS in CRFK, SHE and rat hepatocyte cultures measured by autoradiography. DNA strand breaks were observed with 3 procarcinogens and 4 ultimate carcinogens. Only 2 procarcinogens and 3 ultimate carcinogens could be identified by liquid scintillation counting. A positive autoradiographic response for UDS was observed in CRFK cells with 4 of 5 ultimate carcinogens and 1 procarcinogen. SHE cells showed a positive autoradiographic response for UDS with all ultimate carcinogens and 3 procarcinogens. The autoradiographic system with primary rat hepatocyte cultures was the only one in which a positive response for DNA damage was elicited for all 10 carcinogens.

- 239 AU - ROBERTSON DJ ; GROTH RH ; BLASKO TJ
AD - Instrum. Group, Pratt and Whitney Aircr. Group, Commer. Prod. Div., East Hartford, Conn. 06108, USA.
TI - Organic content of particulate matter in turbine engine exhaust.
SI - HEEP/80/10674
SO - J AIR POLLUT CONTROL ASSOC; 30 (3). 1980. 261-266.
AB - HEEP COPYRIGHT: BIOL ABS. Solid particulate matter, mainly C, emitted into the air from the combustion of fossil fuels contains a variety of organic species adsorbed on it. In an examination of these particulates from the combustion of kerosene type fuels in a gas turbine engine, attention was focused on polynuclear aromatic (PNA) compounds, phenols, nitrosamines and total organics. Polynuclears were determined by HPLC (high performance liquid chromatography), GC/MS (gas chromatography/mass spectrometry) and NMR examination. Phenols and nitrosamines were isolated and measured by GC using a flame ionization detector and N detector. Total organics were determined by a backflush chromatographic procedure. The particulates were collected using a high capacity pumping system and 293 mm diameter teflon filters through which passed up to 43 m3 of exhaust gas. Extraction of the organic matter was done in a Soxhlet extractor usually using hexane. The engine was operated at idle, approach, climb and takeoff power settings with low S and high S (0.25%) fuels. Most of the PAH (polyaromatic hydrocarbons) were small 3 and 4 fused ring compounds with very few, at low concentrations, of 5 and 6 fused ring species. No nitrosamines were found and except in a few cases, at low levels, no phenols. PNA and total organic levels decreased with increase in a power setting and were higher in the exhaust from low S fuels. Less than 1% of the organic matter emitted by the engine was absorbed on the particulate matter.

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are important variables in assessing the potential effect of microsomal enzyme-inducing agents on the metabolism of mutagenic substances.

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- 14 AU - Metivier H ; Masse R ; L'Hullier I ; Lafuma J
AD - Lab. Toxicol. Exp., Inst. Prot. Sante Nucl., Montrouge
TI - Study of the combined action of inhaled plutonium oxide and two chemical carcinogens present in the environment
SI - CA/095/019358F
SO - Biol. Implic. Radionuclides Released Nucl. Ind., Proc. Int. Symp.; VOL 2., 1979,93-104
LA - FRE
AB - CBAC COPYRIGHT: CHEM ABS The modifications of risk attributable to benzo(a)pyrene (I) and dimethylnitrosamine (DMN) following inhalation of PuO2 were studied in rats. (50-32-8 benzo(a)pyrene)(62-75-9 Dimethylnitrosamine) I (2 times, 5 mg) was given intratracheally in assocn. with Fe2O3, 2 and 3 wk after inhalation of PuO2. DMN (2 or 20 ppm) was added to the animals' drinking water. For I, a strong synergistic effect occurred which manifests itself in a substantial redn. of lifetime in animals that have inhaled a small quantity of PuO2 (17 nCi), and in a greater incidence of tumors and enhanced tumor invasiveness whatever the dose of PuO2 inhaled. Inhalation of PuO2 assocd. with regular ingestion of DMN multiplies the metastases of liver cancers in the lung. Addn. of I or DMN modifies the histol. profile of radiation-induced tumors. The synergistic effects are no longer obsd. when the pollutant concns. used produce subacute intoxication.
- 15 AU - Carver JH ; Adair GM ; Wandres DL
AD - Lawrence Livermore Lab., California Univ., Livermore
TI - Mutagenicity testing in mammalian cells. Multiple drug-resistance markers
SI - CA/093/216146V
SO - Report; ISS EPA-600/7-79-173, UCID-18599; Order No. PB80-183114,, 1979,79 pp.
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Chinese hamster ovary (CHO) cell lines heterozygous at the adenine phosphoribosyltransferase (aprt) and thymidine kinase (tk) loci were isolated and used for single-step selection of spontaneous and induced mutants resistant to 8-azadenine (AAR), 6-thioguanine (TGR), 5-fluorodeoxyuridine (FUDR), or ouabain (OUAR). Mutation data are reported for direct mutagens Et methanesulfonate (EMS), N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), 4-nitroquinoline-1-oxide (NQO) and for promutagens dimethylnitrosamine (DMN) and benzo(a)pyrene (BaP) activated by rat liver homogenates. (62-50-0 Ethyl methanesulfonate)(70-25-7 N-Methyl-N'-nitro-N-nitrosoguanidine)(56-57-5 4-Nitroquinoline-1-oxide)(62-75-9 Dimethylnitrosamine)(50-32-8 Benzo(a)pyrene) Crit. plating densities were established for AAR, TGR, and FUDR. Optimal expression of mutant phenotypes after mutation induction with EMS, DMN, or BaP were 2 to 4 d for AAR, 6 to 8 d for TGR, 3 d for OUAR, and 1 to 3 d for FUDR. The induced mutant frequencies as a function of relative cell survival after treatment with EMS, DMN, or BaP showed

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Total binding might indicate a higher carcinogenic potency than was actually obsd.

- 20 AU - Dunkel VC
AD - Natl. Cancer Inst., NIH, Bethesda
TI - Collaborative studies on the Salmonella/microsome mutagenicity assay
SI - CA/091/084117H
SO - J. Assoc. Off. Anal. Chem.; VOL 62, ISS 4, 1979,874-82
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Although the Salmonella plate test has been used extensively, a collaborative study was undertaken to det. the interlab. reproducibility of this microbial mutagenicity assay. All chemicals (61) were tested both with and without metabolic activation in *S. typhimurium* strains TA1535, 1537, 1538, 98, and 100. The metabolic activation systems used were derived from the livers of both uninduced and Aroclor 1254-induced Fischer rats, B6C3F1 mice, and Syrian hamsters. Results on 23 of the chems. tested in 3 of the participating labs. showed that 8 were neg. when tested in all labs. and 13 were pos. Two chems. gave pos. results in 2 labs., but were neg. when tested in the 3rd lab.
- 21 AU - Pitts JN Jr
AD - Statewide Air Pollut. Res. Cent., Univ. California, Riverside, Calif.
TI - Photochemical and biological implications of the atmospheric reactions of amines and benzo(a)pyrene
SI - CA/090/181263Q
SO - Philos. Trans. R. Soc. London, Ser. A; VOL 290, ISS 1376, 1979,551-76
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Exposure of glass fiber filters coated with benzo(a)pyrene (I) to 1 part NO2/106 (and a trace of HNO3) in air formed mutagenic nitro derivs. (50-32-8 benzo(a)pyrene) Nonmutagenic perylene (II) under similar conditions gave a moderate mutagen 3-nitroperylene. (198-55-0 Perylene)(20589-63-3 3-Nitroperylene) Under similar expts. 1-nitroperylene was formed from pyrene, another nonmutagen. (5522-43-0 1-Nitroperylene)(129-00-0 Pyrene) The significant reactivity of I, II, and even pyrene with NO2 was also obsd. in the dark as well as I with O3, peroxyacetyl nitrate (PAN) and ambient photochem. smog. (2278-22-0 Peroxyacetyl nitrate) These reactions of polycyclic arom. hydrocarbons strongly suggest the possibility of similar reactions occurring in the environment, possibly to a major degree. In a related study, diethylamine and triethylamine readily formed photochem.smog (i.e., rapid conversion of NO to NO2 and the formation of O3, AcH, PAN and light-scattering particles) when amine-NO-air mixts. were solar irradiated. (109-89-7 diethylamine)(121-44-8 triethylamine) Addnl. small but

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significant amts. of (Et)2NNO were formed in dark from (Et)2NH but destroyed in sunlight. (55-18-5 Diethylnitrosamine) In contrast, (Et)2NNO was initially formed from (Et)3N on irradiation of the gaseous mixts., then photodecompd. Other major compds. formed included dialkylnitramines and substituted amides. Environmental implications are discussed.

- 22 AU - Rao TK ; Stoltz DR ; Epler JL
AD - Biol. Div., Oak Ridge Natl. Lab., Oak Ridge
TI - Lack of enhancement of chemical mutagenesis by saccharin in the Salmonella assay
SI - CA/092/089050H
SO - Arch. Toxicol.; VOL 43, ISS 2, 1979,141-5
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS A purified batch of saccharin (I) was assayed for mutagenicity and comutagenicity by the Ames Salmonella assay. (81-07-2 Saccharin) I was not mutagenic and failed to enhance the mutagenic activity induced by a wide variety of known mutagens. These results do not argue against the tumor-promoter-like activity of I, but only indicate that the Ames Salmonella assay is not capable of detecting I as a promoter of mutagenesis.

SU - Lancer Res; VOL 38, ISS 7, 1976, P2005-10
 LA - Eng
 AB - The metastatic capabilities of well-defined nodular hepatic

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lesions induced by benzo(a)pyrene, ethylnitrosourea, benzidine.2HCl, and diethylnitrosamine were evaluated. Coded liver and lung tissues from 1264 treated C57BL/6J x C3HeB/FeJ F1 mice were assessed independently for the presence of primary nodular lesions and metastases, respectively. Primary lesions were classified according to their size, cell morphology, and growth patterns into hyperplastic, adenomatous, and trabecular nodules. None of the 126 mice bearing hyperplastic nodules had pulmonary metastases. Four of 291 (1.4%) mice with adenomatous nodular lesions showed metastases. In contrast, of the 733 mice bearing the trabecular type of nodular lesions alone or in combination with other lesions 266 (36%) showed pulmonary metastases. The pulmonary metastases were first detected in mice dying between 51 and 60 weeks of age (5%). This rate increased as a function of age at death, reaching an incidence of 51% in mice surviving more than 81 weeks. It was concluded that nodules showing trabecular and the more anaplastic solid sheet type of growths represented bona fide hepatocellular carcinomas in the mouse.

- 53 AU - Preussmann R
 TI - (Environmental carcinogens: mechanisms of action and occurrence. Some aspects (author's transl))
 SI - TOXBIB/78/183349
 SO - Zentralbl Bakteriell (Orig B); VOL 166, ISS 2-3, 1978, P144-58
 LA - Ger
 AB - New aspects on the mechanism of action of known environmental carcinogens are described. These compounds are not active as such, but are bioactivated in the mammalian metabolism via chemically reactive intermediates to electrophilic reactants, forming with information-bearing biopolymers covalent bonds. This change in the genetic code is in agreement with the mutation hypothesis of carcinogenesis. Aflatoxin B1, N-nitroso compounds and benzo(a)pyrene are taken as examples. "Threshold levels", e.g. no-effect-levels derived from animal experiments with all their inherent limitations, are compared with data from human exposure to benzo(a)pyren, aflatoxine, N-nitroso compounds and vinyl chloride. The difficulties of such risk evaluations are discussed.
- 54 AU - von Neding G
 AD - Bethanien Hospital, Moers, West Germany.
 TI - Possible mutagenic properties and carcinogenic action of the irritant gaseous pollutants NO2, O3, and SO2.
 SI - TOXBIB/78/168876
 SO - Environ Health Perspect; VOL 22, 1978, P91-2
 LA - Eng
 AB - Carcinogenic or cocarcinogenic effects of NO2, O3, and SO2 have not been proven to date with sufficient reliability. However, nitrosamine formation after exposure to NO2- or O3-induced decrease in benzpyrene hydroxylase are potential hazards. A final reevaluation of a possible cocarcinogenic action of SO2 requires further experimental studies.

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for a long period is unusual. In comparison in analogous expts., unchanged polycyclic arom. hydrocarbons (PAH) disappeared practically completely by 5-6 h after administration. The concn. of I after maternal administration, in contrast to PAH, was several-fold lower in the liver of the mother than that in the embryo.

- 56 AU - Robertson DJ ; Groth RH ; Blasko TJ
 AD - Pratt and Whitney Aircr. Group, East Hartford
 TI - Organic content of particulate matter in turbine engine exhaust
 SI - CA/093/030970D
 SO - Proc., Annu. Meet. - Air Pollut. Control Assoc.; VOL 71st. Vol. 2., 1978,78-26.6, 16 pp.
 LA - ENG
 AB - CBAC COPYRIGHT: CHEM ABS Particulate matter from a gas turbine engine was collected for the detn. of org. matter. Org. matter in particles was >1% of the total orgs. emitted. Nitrosamine and phenols were found in only 2 samples. (35576-91-1 Nitrosamine) Most of the polynuclear arom. hydrocarbons (PAHs) had 3 or 4 fused rings and a few had 5 or 6. The total orgs. and PAHs decreased with increase in engine power. PAHs were high in the exhaust from low-S fuels.
- 57 AD - Div. Chem. Carcinog., Inst. Cancer Res., Peking
 TI - Further study on the etiology of esophageal cancer
 SI - CA/093/020427T
 SO - Chung-hua I Hsueh Tsa Chih (Peking); VOL 58, ISS 10, 1978,593-7
 LA - CHI
 AB - CBAC COPYRIGHT: CHEM ABS Environmental factors responsible for a high incidence of esophageal cancer in Lin country (in northern China) were investigated. High concns. of nitrates, nitrites, secondary amines, nitrosamines, and a low level of Mo were found in the environment (drinking water, food, etc.). Some mycobacteria found in food reduced nitrates to nitrites, and hydrolyzed proteins to secondary amines, which promoted the formation of carcinogenic nitrosamines. DMN, diethylnitrosamine,

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methylbenzyl nitrosamine, and N-3-methylbutyl-N-1-methylacetyl nitrosamine were found in contaminated food. (62-75-9 Dimethylnitrosamine)(55-18-5 Diethylnitrosamine)(937-40-6 Methylbenzyl nitrosamine)(71016-15-4 N-3-methylbutyl-N-1-methylacetyl nitrosamine) In in vitro expts., inoculation of *Fusarium moniliforme* on corn in the presence of nitrites resulted in the formation of these carcinogenic substances. The atm. content of benzo(a)pyrene (I) during winter was .10req.17.36 mug/100 m3. (50-32-8 Benzo(a)pyrene) Thus, multiple factors may be responsible for the high incidence of esophageal cancer.

- 58 AU - Tanaka T ; Kono-Tanaka K
 AD - Lab. Cell Biol., Aichi Cancer Cent. Res. Inst., Nagoya
 TI - The effect of cocarcinogen on transplacental carcinogenesis
 SI - CA/092/089064U
 SO - Proc. Perugia Quadrenn. Int. Conf. Cancer; VOL 6th, ISS Tumours Early Life Man Anim., 1978,963-71
 LA - ENG
 AB - CBAC COPYRIGHT: CHEM ABS Rats transplacentally exposed to 5 mg dimethylnitrosamine/kg on the 17th, 18th and 19th days of gestation developed tumors, while animals receiving the dose only on the 17th day produced no tumors. (62-75-9 Dimethylnitrosamine) Nitrosomethylurethane at 10 mg/kg given on the 17th day of gestation did not cause tumors in the offspring while Me methanesulfonate at 8 mg/kg provoked few tumors in the offspring. (615-53-2 Nitrosomethylurethane)(66-27-3 Methyl methanesulfonate) Prenatal exposure to 3 mg benzo(a)pyrene (I)/kg and postnatal treatment with 20 mg diethylnitrosamine/kg and 5 mg Me methanesulfonate/kg caused no tumors. (50-32-8 Benzo(a)pyrene) Combined exposure to 2 carcinogens in prenatal then postnatal life caused a dramatic increase in tumors. Dodecane and phenyldodecane applied topically to progeny of animals treated with I, chrysene, or benzo(b)triphenylene on the 17th day of gestation produced tumors in the offspring.

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- 136 AU - Somogyi A ; Malick LE ; Langenbach R ; Sallach K
 TI - (Contemporary animal nutrition and its potential hazards to human health (author's transl))
 SI - TOXBIB/77/107592
 SO - Zentralbl Bakteriolo (Orig B); VOL 163, ISS 1-4, 1976, P153-72
 LA - Ger
 AB - The growing challenge to secure wholesome food of animal origin in quantities sufficient to feed the ever increasing world population leads to the compelling need of search for new means to enhance animal production. Such an endeavor often involves the use of pharmacologically active agents. As new substances are continuously introduced into agriculture, the necessity clearly arises to reassess the requirements for the approval of compounds likely to appear in the food of man via the edible tissues of animals. Since a number of animal drugs and feed additives have been recently found to show carcinogenic potency, using examples from their own research, the authors discuss problems encountered while planning animal studies for the safety evaluation of chemicals. Among the most important factors to be reckoned with is the metabolism of the test substance. Most carcinogens require metabolic transformation in order to react with macromolecules and, thus, exert their biological action. Similarly, residues of many drugs in animal tissues appear to be various metabolites rather than the parent compounds themselves. At present, it is not known whether many chemical residues are simply stored in different compartments of the carcass as a result of their physico-chemical properties or whether they are covalently bound to vital macromolecules (e.g., nucleic acids). Hence, their biological significance is not quite clear. The enzyme system which metabolizes numerous drugs, pesticides, as well as other endogenous and exogenous substrates is responsible for both the activation and detoxification of carcinogenic chemicals. The delicate balance between these two processes of opposing toxicological consequence is determined by genetic and environmental factors. Depending upon the metabolic profile of chemicals, certain compounds are carcinogenic in one animal species while not in others. The manipulation of their metabolism by physiological (e.g., stress) or pharmacological (e.g., inducers or inhibitors of microsomal enzymes) means can result in a profound change of various biological actions of chemicals (e.g., cytotoxicity, carcinogenicity, mutagenicity). To ascertain that potential toxicological hazards to human health by animal drugs and feed additives will be recognized during the phase of testing, appropriate test animals have to be selected with great care. It is indispensable that the metabolic break-down of the investigational substance proceeds via similar pathways in both test animals and the target species. This will assure that the same metabolites which, in the form of residues in food, man might be exposed to will have ample opportunity to exert their possible adverse effects to the experimental animals during a life-long feeding of the test substance. Therefore, it can, with a reasonable certainty, be assumed that, in experiments performed

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under such precautionary measures, toxico-pharmacological properties relevant to human safety evaluation will not remain undetected.

- 137 AU - Thust R
 TI - Screening of potential chemical carcinogens by means of mammalian cells in vitro.
 SI - TOXBIB/77/086605
 SO - Arch Geschwulstforsch; VOL 46, ISS 7, 1976, P538-48
 LA - Eng
 138 AU - Hard GC ; Grasso P
 TI - Nephroblastoma in the rat: histology of a spontaneous tumor, identify with respect to renal mesenchymal neoplasms, and a

45. MORTALITY PATTERNS IN EIGHT U. K. OIL REFINERIES.

Alderson M, Rushton L
Inst. Cancer Res., Sutton, Surrey, England
Ann NY Acad Sci; 381:139-145 1982

The patterns of mortality are described for 35,000 male employees, with a minimum of 1 year's continuous service, who worked at 8 refineries in the UK in the period 1 January 1951-31 December 1975. The trace rate of those involved was 99.8%. Overall the ratio of observed to expected deaths was 0.84 (O = 4,406, E = 5,259.9 p less than 0.00001). The numbers of deaths for many of the chronic degenerative diseases were lower than 'expected'. The number of observed deaths from all cancers were appreciably less than expected (O = 1,147, E = 1,286.4, O/E = 0.89, p = 0.00006). Lung cancer was particularly reduced (O = 416, E = 532.7, O/E = 0.78, p 0.00001); there was no excess of leukemia (in workers including some exposed to benzene). Other comparable studies have suggested an excess of gastrointestinal cancer. In the present study deaths from esophageal, stomach, intestinal, and rectal cancer were slightly raised for all workers (O = 346, E = 328.6, O/E = 1.05, p less than 0.4); this was particularly true for those joining before 1950 with long service and increased latent interval. There were also excesses based on small numbers of deaths from nasal cancer (O = 7, E = 3.1, O/E = 2.24, p less than 0.05), and melanoma (O = 14, E = 6.5, O/E = 2.16, p less than 0.01). There was no evidence of an excess of brain tumors (O = 36, E = 44.8, O/E = 0.80, p less than 0.2). (Author abstract) (18 Refs)

46. BRAIN CANCER: ISSUES AND DILEMMAS.

Hanis NM, Holmes TM, Newill VA, Smith FR, Smith LG
Exxon Corporation, East Millstone, NJ, 08873
Ann NY Acad Sci; 381:83-90 1982

A cohort study covering the 8 yr period, 1970-1977, identified eight deaths attributed to brain cancer among employees at a refinery/chemical plant. Five of the cases were primary brain cancers and three were either metastatic from another site or the site was undetermined. A ninth case of brain tumor unspecified was identified. Five primary brain cancers would have been expected, based on national statistics. Some issues and dilemmas related to such a cohort study were discussed. (Author abstract) (4 Refs)

47. CORRELATION OF OCCUPATION AND KARYOTYPE IN ADULTS WITH ACUTE NONLYMPHOCYTIC LEUKEMIA.

Golomb HM, Allmena G, Rowley JD, Vardiman JW, Testa JR, Sovik C
Box 420, 950 East 59th St., Chicago, IL, 60637
Blood; 60(2):404-411 1982

Seventy-four adult patients with acute nonlymphocytic leukemia (ANLL) were classified retrospectively as to whether or not they had had occupational exposure to insecticides, chemicals and solvents, or petroleum products. Fifty-eight patients were considered nonexposed and 16 were considered exposed. The chromosome banding pattern was abnormal in 37 of the 74 patients (50%). Twenty-five of the 58 (43%) nonexposed patients had a clonal chromosome abnormality, compared with 12 of the 16 (75%) exposed patients (p = 0.02). Only 2 of 23 (8.7%) females with an abnormal karyotype were exposed, whereas 10 of 14 (71%) males with an abnormal karyotype were exposed. Either a-5/5q- or a-7/7q- was present in 67% of the exposed patients with a chromosome abnormality, com-

pared to 28% of the aneuploid nonexposed patients. The-7/7q- abnormality was present in 7 of the 12 (58.3%) exposed patients, vs 5 of the 25 (20%) nonexposed patients with abnormal karyotypes (p less than 0.05). The-5/5q- anomaly was observed in 4 of the 12 (33%) exposed patients and in 4 of the 25 (16%) nonexposed abnormal patients. Our study supports the observation that a subset of patients with ANLL de novo have a history of occupational exposure and a unique pattern of chromosome abnormalities. (Author abstract) (18 Refs)

48. CANCER MORTALITY AMONG THREE SWEDISH MALE ACADEMIC COHORTS: CHEMISTS, ARCHITECTS, AND MINING ENGINEERS/METALLURGISTS.

Olin GR, Ahlborn A
Preventive Occupational Medicine Unit, Royal Inst. Technology, S-100 44 Stockholm, Sweden
Ann NY Acad Sci; 381:197-201 1982

Cancer mortalities were investigated in three cohorts of professionals graduating from the same academic institution during the same period of time (1930-59). The study included 820 chemists, 581 mining engineers, and 657 architects, of which 83, 49, and 59, respectively, were deceased. Standard mortality ratios comparing the three groups to the overall Swedish male population showed that all of them had ratios well below 100. Relative risk rates were not significantly different among the three groups. The neoplasm rate differed among the cohorts, with the relative risk for chemists being 2.5 x that of architects and for mining engineers 1.8 x. The difference in neoplastic mortality between the architects and chemists seems to be due to different rates of death among two neoplastic code-groups: leukemia/lymphoma (including 3 cases of Hodgkin's disease), and glioma. Of 32 neoplastic deaths among the chemists, 5 were attributed to gliomas. Methyl nitrosourea was used routinely without special precautions for diazotization in Swedish educational laboratories up until the middle 1960's, but the significance of this fact to the present results has not been determined. (8 Refs)

49. BRAIN AND CENTRAL NERVOUS SYSTEM CANCER MORTALITY IN U. S. RUBBER WORKERS.

Symons MJ, Andjelkovich DA, Spirtas R, Herman DR
Occupational Health Studies Group, Sch. Public Health, Univ. North Carolina, Chapel Hill, NC, 27514
Ann NY Acad Sci; 381:146-159 1982

Since 1963 the observed mortality experience of BCNS cancers among rubber workers appears to be very comparable to that expected. A possible exception to this statement is the experience of one plant in Akron, Ohio, reported by Monson and Nakano. Excesses in earlier years may also be localized to one or two companies. The results of a case-control study did not support a hypothesized association of elevated BCNS cancer risk with exposures in the tire building/tire assembly segments of the rubber tire manufacturing process. The direction of future epidemiologic studies would benefit by the assembly of as large a number of cases as possible and should focus on calendar periods of exposure, make allowance for a latent period, and include retrospective industrial hygiene assessments of the specific exposures. (Author abstract) (28 Refs)

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54. A CASE-CONTROL STUDY OF CHEMICAL EXPOSURES AND BRAIN TUMORS IN PETROCHEMICAL WORKERS.

Amesin SP, Schnatter AR
Dept. Epidemiology, Union Carbide Corporation, Old Ridgebury Road,
Danbury, CT, 06817
JOM; 25(4):313-320-1983

The relationship between chemical exposures and deaths attributable to primary brain tumors among employees of a Texas petrochemical plant was investigated. Cases consisted of 21 deaths in which the underlying cause was confirmed as a primary brain tumor. Two control groups of 80 employees each were randomly selected from 450 decedents known to the company in June, 1979. Potential exposures while employed were compared between cases and controls for five known or suspect carcinogens. Exposure potentials were also compared for an additional 37 chemicals to which at least four cases were potentially exposed. Overall and 15-yr latency analyses were performed. The proportion of cases exposed to the five potentially carcinogenic chemicals (including vinyl chloride) were lower than or consistent with the proportion of exposed controls. No statistically significant differences between the proportions of cases and controls exposed to the 37 other chemicals were found. (Author abstract) (10 Refs)

55. POSSIBILITIES FOR IDENTIFYING GENOTOXIC RISKS IN THE RUBBER INDUSTRY: USE OF THE URINARY MUTAGENICITY ASSAY AND SISTER CHROMATID EXCHANGE.

Vainio H, Falck K, Maki-Paakkanen J, Soraa M
Department of Industrial Hygiene and Toxicology, Institute of Occupational Health, Helsinki, Finland.
IARC Sci Publ; (32):571-7 1982

Two approaches have been used for biological monitoring of exposure to genotoxins in the rubber industry: (1) assay of mutagenic activity in urine with the bacterial fluctuation test; and (2) analysis of sister chromatid exchange frequencies in peripheral blood lymphocytes. Workers in the rubber industry have significantly more mutagenic activity in their urine than nonexposed controls. Mutagenic activity was tested with *Escherichia coli* WP2 uvrA as indicator bacteria was significantly higher in urine of workers after a normal work week than in urine samples from the same individuals after a holiday. The mean frequency of sister chromatid exchange in rubber workers who smoked was significantly higher (p less than 0.01) than that in unexposed smokers. The only job categories in which workers who smoked had statistically significantly higher mean frequencies than others were mixing and weighing. People in these jobs generally also had high mutagenic activity in their urine. (Author abstract)

56. INCIDENCE OF LUNG CANCER AND AGE AT DEATH IN SILICOSIS DEATHS OF THE SWISS NATIONAL ACCIDENT INSURANCE FUND, 1960-1978

Schuler G, Walchi P, Ruttner JR, Delmore M, Taylor M, Schnieper R
Zürcher Arbeitsgemeinschaft zur Erforschung und Bekämpfung der Staublungen in der Schweiz.
Soz Präventivmed; 27(5):218-9 1982

The frequency of lung carcinoma among the deaths of silicotics registered by the Swiss National Accident Insurance Fund from 1960 to 1978 has been compared with the causes of death of all Swiss males during the same period. The PMR, while underestimating the true risk, is significantly raised among foundry workers. SMR's for lung cancer (estimated by com-

paring the numbers of pulmonary and non-pulmonary malignancies) are elevated among foundry workers, miners, workers in ceramic and miscellaneous industries. Only the stone/slate industry has not yielded a significant excess of lung cancers. (Author abstract) (In GER)

57. ORGANIC SOLVENTS—AN INCREASING PROBLEM IN THE OCCUPATIONAL ENVIRONMENT

Hansen L
Frederiksberg hospital, DK, Kbenhavn.
Nord Med; 97(12):299-301 1982

Keywords (MeSH): Abnormalities, Drug-Induced/etiology; Brain/drug effects; Female; Human; Male; Neoplasms/chemically induced; Occupational Diseases/*chemically induced; Pregnancy; Solvents/*adverse effects.

58. A CASE-REFERENT STUDY ON NASAL CANCER AND EXPOSURE TO WOOD DUST IN THE PROVINCE OF SIENA, ITALY.

Battista G, Cavallucci F, Combe P, Quercia A, Vindigni C, Sartorelli E
Istituto di Medicina del Lavoro, Via dei Tuffi 1, Siena, Italy
Scand J Work Environ Health; 9(1):25-29 1983

The aim of the present study was to assess the risk of nasal cancer associated with exposure to dust in the wood and furniture industry in the province of Siena, Italy. Four to seven percent of the active male population is employed in this sector. A case-referent approach was used. The cases included male subjects seen at the Ear, Nose and Throat Clinic and the Radiotherapy Unit of Siena and diagnosed as having cancer of the nasal cavities or paranasal sinuses between 1963 and 1981. The referents were male patients admitted to the Medical Clinic of Siena for all causes except nasal neoplasia; they were matched 5:1 to the cancer patients for age and time of admission. Information was gathered (by postal questionnaires) on the occupational histories of all 36 of the cancer patients and 164 of the 180 referents. The odds ratio associated with exposure to wood dust was 5.4 (1.7-17.2) for all carcinomas, and 89.7 (19.8-407.3) for mucinous adenocarcinoma. The woods used by the exposed cancer patients were mainly oak, chestnut, poplar, and fir. The median duration of exposure was 40 years; no exposed cancer patient reported the presence of exhaust systems in their work environment. (Author abstract) (13 Refs)

59. LEUKEMIA IN HOSPITAL PATIENTS WITH OCCUPATIONAL EXPOSURE TO THE SAWMILL INDUSTRY [LETTER]

Burkart JA
West J Med; 137(5):440-1 1982

Keywords (MeSH): Adult; Aged; Human; Leukemia/*etiology; Male; Middle Age; Occupational Diseases/*etiology; Wood.

URL 14153

REVIEWS INCLUDING NITROSO COMPOUNDS

33. FORMATION OF METHYLAMINES FROM INGESTED CHOLINE AND LECITHIN.

Zetzel SH, Wishnok JS, Blaszczak JK

Department of Pathology, Boston University School of Medicine, Massachusetts.

J Pharmacol Exp Ther; 225(2):320-4 1983

Humans ingest substantial amounts of choline and lecithin as part of common foods. Physicians have recently begun administering large doses of these compounds to individuals with neurological diseases. A significant fraction of ingested choline is destroyed by enzymes within gut bacteria, forming trimethylamine (TMA), dimethylamine (DMA) and monomethylamine (MMA). Some of these methylamines are eventually excreted into the urine, presumably after being absorbed and carried to the kidneys via the bloodstream. The methylamines formed after choline is eaten could be substrates for the formation of nitrosamines, which have marked carcinogenic activity. Twenty-seven millimoles of choline chloride, choline stearate or lecithin were administered to healthy human subjects. It was found that these treatments markedly increased the urinary excretion of TMA, DMA and MMA, with choline chloride having the greatest effect. Rats were treated with 2 mmol/kg b.wt. of choline chloride or lecithin, and it was found that these treatments significantly increased urinary TMA excretion and did not alter DMA or MMA excretion. Our choline chloride preparation contained no MMA, DMA or TMA; however, it was found that our choline stearate and all the commercially available lecithins tested were contaminated with methylamines. Prior removal of methylamines from our lecithin preparation minimized the effect of oral administration of this compound on methylamine excretion in urine of rats and humans. (Author abstract)

34. THE URINARY BACTERIAL FLORA IN PATIENTS WITH THREE TYPES OF URINARY TRACT DIVERSION.

Hill MJ, Hudson MJ, Stewart M
Bacterial Metabolism Research Laboratory, PHLS Centre for Applied Microbiology and Research, Wiltis, London.
J Med Microbiol; 16(2):221-6 1983

There is known to be a high risk of malignancy at uretero-colic anastomoses and it has been postulated that bacteria catalyse both the local formation and the activation of carcinogens such as N-nitrosamines. If this theory is correct, then the risk of malignancy should be greatest when the prevalence of mixed urinary tract infection is greatest. Bacterial culture was performed on samples of urine obtained from 56 patients with three forms of urinary tract diversion: ureterosigmoidostomy, isolated ileal and colon conduits. As expected, the rectal urine of all patients with a ureterosigmoidostomy had a rich bacterial flora. However, 11 of the 15 patients with ileal conduits (73%) had significant mixed growths of bacteria in the loop urine, whereas only six out of 16 colon loop urines (37.5%) were infected, all being monobacterial infections. The implications of these bacteriological findings for carcinogenesis associated with urinary diversion are discussed. (Author abstract)

35. CANCER AND SECONDARY LEUKEMIA.

Rosner F
Queens Hospital Center Affiliation of the Long Island Jewish-Hillside Medical Center, Jamaica, New York.
Bull Cancer (Paris); 70(1):55-60 1983

Acute myeloid leukemia or one of its variants is being reported with increasing frequency as a second neoplasm in patients being treated for multiple myeloma, Hodgkin's disease, non-Hodgkin's lymphoma and a variety of other primary neoplasms and non-neoplastic diseases. Although many of these patients were treated with both chemotherapy and radiotherapy, many received no radiotherapy at all. Drugs most frequently implicated in the causation of acute leukemia and other second neoplasms are the alkylating agents, procarbazine and the nitrosoureas. The frequency of this syndrome varies from less than 1 per cent to 7 per cent in many reported series of patients. There could develop a reluctance to use cytotoxic agents to treat malignant neoplasms for fear of inducing acute leukemia. Although one has to consider this complication, one should not, however, withhold these drugs from a patient with a neoplasm or other potentially fatal disease in whom such therapy is the treatment of choice. We seem to be faced with the paradox that patients benefiting most from chemotherapy may be at highest risk of suffering its undesirable consequences. Although the risk of leukemogenesis or carcinogenesis in man may be small, these drugs should be used with caution in patients with indolent non-neoplastic diseases such as rheumatoid arthritis. (Author abstract)

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87. INHIBITION BY ALCOHOLS OF THE LOCALIZATION OF RADIOACTIVE NITROSONORNICOTINE IN SITES OF TUMOR FORMATION.

Waddell WJ, Marlowe C
Department of Pharmacology and Toxicology, University of Louisville,
Kentucky.
Science; 221(4605):51-3 1983

Oral administration of ethanol, n-butanol, or t-butanol to mice 20 minutes before injection of carbon-14-labeled nitrosonornicotine inhibited the localization of radioactivity in bronchial and salivary duct epithelium and in the liver. Localization of radioactivity in the nasal epithelium and esophagus was not significantly reduced. These alcohols therefore may selectively inhibit tumor formation in three of the five sites where this carcinogen typically acts. (Author abstract)

88. MECHANISM OF CO-CARCINOGENIC ACTION OF ETHANOL ON NITROSAMINE CARCINOGENESIS IN RAT LIVER (MEETING ABSTRACT).

Schwarz M, Bachmann A, Kunz W
Institute of Biochemistry, German Cancer Research Center, D-6900
Heidelberg, W. Germany
Symposium on Role of Carcinogens and Promoters in Human and Experimental Carcinogenesis, May 16-18, 1983, Budapest, Hungary
Hungarian Cancer Society, 1983.

Chronic consumption of alcohol containing beverages is associated with an increased risk in cancer of various organs including the liver. Ethanol by itself appears to show no carcinogenic potential but may possess co-carcinogenic or tumor-promoting activity. In contrast to the results of in vitro studies ethanol does not interfere with the activation metabolism of the model carcinogen dimethylnitrosamine in vivo. However, simultaneous treatment of rats with ethanol and carcinogen leads to an increase in number and especially in size of ATPase-deficient preneoplastic foci in liver induced by either diethylnitrosamine or nitrosomorpholine. The alcohol levels used in these experiments were found to markedly increase DNA synthesis in liver. Enhancement of preneoplastic response, which seems to be limited to ethanol doses associated with such an increase in DNA synthesis, may be referred to by definition as co-carcinogenic action. At this dose level however, ethanol does not show any promoting activity in liver. When given after cessation of carcinogen treatment following a tumor-promotion feeding protocol the extent of enzyme-deficient areas was found to be rather decreased. Ethanol treatment does not lead to any enhancement in the total amount of liver DNA with concomitant liver growth. The observed increase in DNA synthesis might therefore be due to an acceleration of cell turnover as a consequence of the known hepatotoxic action of alcohol. The significance of this stimulus of regenerative DNA synthesis induced by ethanol seems to differ from that of known tumor-promoting drugs (eg phenobarbital) which result in an increase in the total amount of liver DNA. Chronic liver regeneration induced by ethanol therefore only leads to an increase in risk when the alcohol acts in the presence of a liver carcinogen. (1 Ref)

89. INFLUENCE OF ETHYL-ALCOHOL ON CARCINOGENESIS INDUCED WITH N-NITROSODIETHYLAMINE (MEETING ABSTRACT).

Griciute L, Castagnaro M, Berezniat JC
Oncological Research Institute of Lithuanian SSR, Vilnius, Russia
Symposium on Role of Cocarcinogens and Promoters in Human and Experimental Carcinogenesis, May 16-18, 1983, Budapest, Hungary
Hungarian Cancer Society, 1983.

Small quantities of N-nitrosodiethylamine (NDEA) are being commonly detected in strong colored beverages. Some of these are believed to increase the morbidity of mouth and esophagus cancer in humans. The aim of our experiment was to establish whether ethyl alcohol, used as a solvent, influences the carcinogenic activity of NDEA. Two hundred twelve mice C57 Bl, male or female have been divided into 3 groups: I gr intragastric instillations of 0.03 mg of NDEA in 40 degree ethanol was administered twice a week for 50 weeks; II gr the same dose of NDEA in tap water has been administered at the same time; III gr control 40 degree ethanol was given. A lot of benign and malignant tumors have been detected in groups I and II, but only several in group III. The forestomach tumor was the main tumor attributable to NDEA. This cancer developed in about 40 per cent of animals in the I ethanol group and about 10 per cent in the II water-group. Apart from this a big part of forestomach cancers in the I group, but none in the II group, metastasized in lungs, liver and other sides. There were no forestomach cancers in control group. In conclusions: ethanol used as a solvent enhanced both cancerogenic activity of NDEA and progression of tumors. The mechanism of this phenomenon is being studied. (no Refs)

90. DIETARY LIPID EFFECTS ON THE GROWTH, MEMBRANE COMPOSITION, AND PROLACTIN BINDING CAPACITY OF RAT MAMMARY TUMORS (MEETING ABSTRACT).

Cave WT, Jurkowski JJ
Univ. of Rochester Medical Center, Rochester, NY, 14611
Proc Am Assoc Cancer Res; 24:685 1983

The purpose of this study was to evaluate the effects of qualitative as well as quantitative differences in dietary lipid on mammary tumor growth and to examine some of the mechanisms that might be involved. Female F-344 rats were divided into 5 dietary groups: (a) 0.5% corn oil, (b) 3% corn oil, (c) 3% corn oil + 17% lard, (d) 20% corn oil, (e) regular lab chow (approx 6% lipid). All animals were simultaneously administered the carcinogen nitrosomethylurea and those developing tumors were killed when their tumors exceeded 2 cm in diameter. Specific prolactin (PRL) binding measurements were then performed on the microsome membrane fractions of these tumors and their fatty acid profiles were determined by gas chromatography. We conclude that (1) once the dietary polyunsaturated fat content of the diet exceeds 3%, it is the total amount of lipid in the diet rather than the type that determines the ultimate mammary tumor growth rate (2) reductions in dietary polyunsaturated fat below 3% are associated with reductions in mammary tumor growth (3) alterations in the specific binding of prolactin to mammary tumor membranes seem most closely related to this latter process and less so with variations in tumor growth caused by diets containing more than 3% polyunsaturated fatty acid. (no Refs)

did not cause a change in diet (eg, fractures) was almost identical to that among population controls. These results suggest that, in hospital-based case-control studies of the effects of coffee consumption, it would be prudent to restrict the referent group to those patients hospitalized for conditions that probably did not cause a change in diet. The magnitude of bias resulting from failure to exclude controls hospitalized for diet-altering conditions will depend on two factors that may vary between studies: (1) the distribution of diet-altering conditions among the hospital controls, and (2) the relationship of these diseases to coffee consumption. (Author abstract)

177. THE LOUISIANA CANCER CONTROVERSY: SOME SCIENTIFIC PERSPECTIVES.

Carlo GL, Carrier MF, Flanagan KJ
United States Area Medical, 1803 Building, Dow Chemical U.S.A.,
Midland, MI, 48640
J La State Med Soc; 135(3):8-9,11-13,16 1983

Possible misconceptions regarding the cancer death rate in Louisiana are discussed. Information sources on the cancer rates in Louisiana include cancer mortality maps, data gathered through the Surveillance, Epidemiology, and End Result Program and the epidemiological studies. It is suggested that errors could occur through differences between the numerators or denominators of rates from different geographic areas which result in differential rates, differences in age distribution of the population, differences in survivorship, and differences in incidence of disease. (8 Refs)

178. HETEROGENEITY IN HISTORICAL COHORT STUDIES: A SOURCE OF BIAS IN ASSESSING LUNG CANCER RISK.

Weiss W
Div. Occupational Medicine, Hahnemann Univ. Sch. Medicine, 230 N.
Broad St., Philadelphia, PA, 19102
JOM; 25(4):290-294 1983

Historical cohorts that are heterogeneous with respect to era in which exposure to a hazard began are subject to chronology bias. Those historical cohorts assembled some time after onset of exposure are also subject to selection bias through attrition of the original populations prior to the time of registration. Such cohorts may be called multiserial cross-sectional. The two forms of bias in such cohorts may account for some of the elevated risk of lung cancer reported in occupational studies of this type. Historical cohorts comprising all workers who began exposure in a relatively limited era can be called inception cohorts. Three occupational investigations are reviewed in which both multiserial cross-sectional cohorts and inception cohorts were studied. In all three investigations the inception cohorts showed lower risks of lung cancer than the multiserial cross-sectional cohorts. (Author abstract) (7 Refs)

179. RELATIONSHIP BETWEEN BODY WEIGHT AND THE INCIDENCE OF POSITIVE AXILLARY NODES AT MASTECTOMY FOR BREAST CANCER.

Zamoff B, Dasgupta I
Clinical Research Center, Montefiore Hospital and Medical Center,
Bronx, New York.
J Surg Oncol; 22(4):217-20 1983

The question, whether obesity is associated with an increased incidence of positive axillary nodes at mastectomy for breast cancer, was studied in two quite different hospital populations; one from a large urban teaching hospital (Montefiore) and one from a medium-sized Air Force medical center (Mal-

colm Grow). In the Montefiore population, the answer was 'yes'; 67% of the node-positive patients, but only 31% of the node-negative patients were obese (20% or more above ideal weight) (p less than 0.05). In the Malcolm Grow population, the answer was 'no'; 20% of the node-positive and 20% of the node-negative patients were obese. The different answers, we believe, are due to the biological differences between the populations; the Montefiore population was shorter (by an average of 1.7 inches), heavier (by an average of 20 lbs), and more obese. The incidence of obesity was about three times as high in the Montefiore population (52% versus 20%; p less than 0.02) and it contained a statistically distinct subpopulation of obese patients, while the few obese patients in the Malcolm Grow population constituted merely the upper tail of a unimodal log-normal distribution of weight in that population. We propose that it is possible to demonstrate a relationship of obesity to node-positivity in the Montefiore population but not in the Malcolm Grow population because obesity was highly prevalent in the former and almost nonexistent in the latter. It seems self-evident that it is not possible to demonstrate an effect of obesity in a population if that population manifests no significant obesity, statistically speaking, but disregarding this principle, we believe, may account for the controversy in the literature about whether obesity is a risk factor in breast cancer. (Author abstract)

180. ISOLATION OF A GROUP AT RISK FOR STOMACH CANCER BASED ON GENETIC AND EPIDEMIOLOGICAL STUDY DATA

Al'tshuler BA, Glazkova TG, Koshcheev VA, Vapnik VN, Prytkov AN
Vopr Onkol; 29(2):8-13 1983

The predictive value of risk factors of stomach cancer was studied on the basis of the results of a complex genetical-epidemiologic survey conducted with a view to identifying the group at risk. An optimal combination of these factors and the multifactor method of mathematical statistics were used in working out a decision instruction. Application of the latter offers an 80% credibility in selecting persons at high risk for stomach cancer development. The paper deals with the findings on a significant relationship between stomach cancer development and genetic and familial factors as well as on indications at certain changes in gastrointestinal function observed before clinical manifestation of the disease. The results point to the efficacy of complex clinical, genetic and epidemiologic studies conducted for prediction of neoplasms caused by a set of factors. (Author abstract) (In Rus)

181. EPIDEMIOLOGIC APPROACHES TO CANCER ETIOLOGY. (76 REFS)

Fraumeni JF Jr
Environmental Epidemiology Branch, National Cancer Institute, Na-
tional Institutes of Health, Bethesda, Maryland.
Annu Rev Public Health; 3:85-100 1982

Keywords (MeSH): Alcohol Drinking; Environmental Pollutants/adverse effects; Epidemiologic Methods; Epstein-Barr Virus/immunology; Estrogens/adverse effects; Human; Immunosuppressive Agents/adverse effects; Neoplasms/chemically induced/*etiology/familial and genetic/occurrence; Neoplasms, Radiation-Induced/etiology; Nutrition; Occupational Diseases/chemically induced; Review; Smoking; Sunlight/adverse effects.

109. CANCER REPORTING IN PAPUA NEW GUINEA: 1958-70 AND 1971-78.

Atkinson L, Purohit R, Reay-Young P, Scott GC
Institute of Oncology and Radiotherapy, Prince of Wales, New South
Wales, Australia.
Natl Cancer Inst Monogr; (62):65-71 1982

In 1958, a cancer registry was established in Papua New Guinea for a population of 2 million who had remained in near isolation for millennia until recently. This report includes cancer data for 1970 through 1978. During those years, the registrations increased from 200 to 600. The reasons for this increase and the patterns of reporting over the entire 21-year period are examined. The data offered us opportunities to examine changes in case findings according to geography, time, and sex. Genuine differences in cancer incidence and pattern within this diverse country, mainly between the highland and lowland regions, were studied, particularly concerning oral, skin, liver, and penile cancers, and Burkitt's lymphoma. The controversy remains over the relationship of oral cancer and chewing of substances other than tobacco; but in this country, at least, a chew consisting only of areca nut mixed with lime must be held suspect. With the emergence from isolation, profound socioeconomic changes are occurring in this country; the patterns of cancer must change also, and we may be seeing the beginning of this already. Possible fruitful areas for further detailed studies are indicated. (Author abstract)

110. CANCER INCIDENCE IN SINGAPORE: 1973-77.

Lee HP, Shanmugaratnam K
Department of Pathology, National University of Singapore, Singapore
General Hospital.
Natl Cancer Inst Monogr; (62):57-60 1982

The Singapore Cancer Registry started operations on January 1, 1968. It is a population-based registry that seeks to obtain basic epidemiological and clinical data on all cases of cancer diagnosed in Singapore. The results presented pertain only to Singapore citizens and permanent residents and cover the period from 1973 to 1977. Of special interest are the cancer patterns of the main ethnic groups in Singapore. Generally, the Chinese (76% of total population) have significantly higher risks for cancer; the most prevalent sites are the nasopharynx, esophagus, stomach, liver, and lung. Within the Chinese group are also dialect group differences. The Malays (15% of population) have the lowest rates for most sites, whereas among the Indians (7% of population), mouth cancer is an important site for both sexes. All these variations provide useful clues in the search for etiological factors. (Author abstract)

111. CANCER PATIENT SURVIVAL: SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS PROGRAM, 1973-79.

Ries LG, Pollack ES, Young JL Jr
Division of Cancer Cause and Prevention, National Cancer Institute,
Bethesda, Md.
JNCI; 70(4):693-707 1983

Data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute were used in the evaluation of cancer patient survival experience for almost 10% of the U.S. population. This first report contains actuarial (life table) survival analysis on 368,263 patients with first primary cancer diagnosed in 1973-79 from nine SEER areas: the entire States of Connecticut, Iowa, New Mexico, Utah, and Hawaii and the metropolitan areas of Atlanta, Detroit, San Francisco, and Seattle. Both observed and relative survival rates were shown for whites and blacks, sex, age, primary site,

and time period (each yr, 1973-78). The largest racial difference in survival was for cancer of the corpus uteri: 87% 5-year relative survival rate for white females versus only 54% for black females. Survival rates varied considerably by primary site. For most sites, as age increased the relative and observed survival rates decreased. Analysis of relative survival rates by each year of diagnosis, 1973-78, and for each year following diagnosis suggested increasing rates for cancers of the colon, lung, and prostate gland, whereas there were no definite increases for cancers of the female breast and corpus uteri. A dramatic increase in survival from acute lymphocytic leukemia was found for children under 15 years of age, with the 4-year relative survival rate increasing from 51% among those diagnosed in 1973-75 to 65% for those diagnosed in 1976-78. (Author abstract)

112. CANCER AND LIFESTYLE IN LOUISIANA.

Correa P, Johnson WD
Dept. Pathology and Biometry, Louisiana State Univ. Medical Center,
New Orleans, LA
J La State Med Soc; 135(3):4-6 1983

A cancer survey of men in southern Louisiana is reported. Respiratory cancer rates among these men are among the highest in the United States. Results of the survey indicated that one-third of the white labor force works in oil and shipbuilding industries and that more river water is used for drinking water in the south. Cigarette smoking is also more prevalent in the south. (5 Refs)

OTHER EPIDEMIOLOGICAL FINDINGS

113. POPULATION STUDIES OF POLYMORPHISM IN DRUG OXIDATION AND ITS RELEVANCE TO CARCINOGENESIS.

Ritchie JC, Idle JR
Department of Pharmacology, St Mary's Hospital Medical School,
London, UK.
IARC Sci Publ; (32):381-94 1982

Metabolic oxidation plays a central role in both the detoxication and chemical activation of many environmental procarcinogens. A plethora of in vitro data suggests that metabolic activation and subsequent DNA covalent binding of such substances vary widely between individuals. The need for a simple test in vivo of human variability in metabolic oxidation is apparent, not only to help understand the variation in disposition of many drugs and other chemicals, but also as an aid to predicting individual cancer risk from metabolically activated procarcinogens. Current methodology has failed to provide such information for a number of reasons, which are discussed. A genetic polymorphism affecting the metabolic disposition and biological effects of a number of drugs is described. Persons can be phenotyped as either extensive or poor metabolizers, using the drug debrisoquine. The measured variable, urinary 'metabolic ratio', which is distributed across these two phenotypes with values of 0.1 to 200, gives a clear indication of the metabolic behaviour of many drugs and, possibly therefore, of certain procarcinogens. Accordingly, two groups of cancer patients were investigated with debrisoquine, namely Nigerians with hepatocellular and related tumours and white smokers with bronchial carcinoma in the United Kingdom. These preliminary studies are suggestive of a phenotype component in relative cancer risk, poor metabolizers appearing to be less vul-

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sociated epithelium in these animals. In addition, we defined the normal distribution of colonic lymphoid patches in both DMH-treated and control rats. Patches were found macroscopically and confirmed by histologic examination at five constant sites: lower pole of cecum, proximal ascending colon, the major colonic flexure, mid descending colon, and the rectosigmoid. There are also the predominant sites of DMH induced carcinomas in W/Fu rats. In 120 DMH-treated animals, 109 colon carcinomas were found. Eight percent were in the lower pole of the cecum, 56% in the proximal ascending colon, 16% at the major flexure, 15% in the mid descending colon, and 5% in the rectosigmoid. Lymphoid patches could often be detected histologically in association with DMH-induced tumors. The depth of tumor invasion was found to correlate inversely with our ability to identify tumor-associated lymphoid patches suggesting that tumors arising at the anatomical sites were lymphoid patches occur progressively destroyed them. Of colon tumors confirmed histologically to be associated with lymphoid patches, 88% were superficial lesions confined to the submucosa and 12% were more extensive but confined to the bowel wall. No lymphoid patches could be found associated with tumors that extended through the bowel wall. Thus, DMH-induced colon carcinomas in W/Fu rats arise at sites containing preexisting LP-GALT with associated specialized epithelium. (Author abstract)

4. EFFECT OF 13-CIS-RETINOIC ACID ON EARLY PRECANCEROUS ANTIGENIC GOBLET-CELL MODIFICATIONS AND INDUCTION OF CANCER DURING 1,2-DIMETHYLHYDRAZINE CARCINOGENESIS IN RATS.

Decaux C, Rosa B, Barn J, Daher N, Burtin P
Laboratoire d'Immunochimie, IRSC, Villejuif, France.
Carcinogenesis; 4(9):1175-8 1983

The possible effect of oral 13-cis-retinoic acid (13-cis-RA) on the carcinogenic process induced by 28 weekly s.c. injections of 1,2-dimethylhydrazine (DMH) in 34 Wistar rats was investigated. Using immunohistology, precancerous and cancerous stages were compared with the same stages induced by DMH without additional 13-cis-RA in 33 rats. M1 antigens, which characterize modifications in goblet-cell differentiation occurring early in rat colonic carcinogenesis, were used to investigate the possible effect of retinoids on differentiation during precancerous stages. From 3-20 weeks after the start of the experiment, no significant differences were observed in the timing of M1 antigens in the 2 groups of rats. It was also observed that 13-cis-RA had no effect on histological lesions associated with precancerous mucosa, nor on the occurrence of intestinal adenocarcinomas. Thus, under these conditions, oral administration of 13-cis-RA did not significantly inhibit precancerous or cancerous stages of intestinal carcinoma development. (Author abstract)

5. TUMORIGENIC ACTION OF REPEATED SUBCUTANEOUS ADMINISTRATION OF N-METHYL-N-FORMYLHYDRAZINE IN MICE.

Toth B, Patil K
Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska, Medical Center, Omaha.
Neoplasia; 30(4):437-41 1983

N-Methyl-N-formylhydrazine (MFH), an ingredient of the edible false morel mushroom, was administered to Swiss mice as 40 weekly subcutaneous injections at 20 micrograms/g body weight for females and 10 micrograms/g body weight for

males. The treatments gave rise to statistically significant incidences of lung tumors: 56% in females and 40% in males. Administration of the chemical resulted in no detectable carcinogenic effect in other organs. The findings are discussed in light of the results from earlier studies with this compound. (Author abstract)

HETEROCYCLIC COMPOUNDS

6. MUTAGENICITIES OF GLYCIDYL ETHERS FOR SALMONELLA TYPHIMURIUM: RELATIONSHIP BETWEEN MUTAGENIC POTENCIES AND CHEMICAL REACTIVITY.

Sugiura K, Goto M
Institute of Ecotoxicology, Gakushuin University, Toshima-ku, Tokyo, Japan.
Chem Biol Interact; 45(2):153-69 1983

The lethal and mutagenic effects of ethyl, benzyl, 1-naphthylmethyl, 2-naphthylmethyl, 1-naphthylethyl, 2-naphthylethyl and 9-anthrylmethyl glycidyl ethers on *Salmonella typhimurium* (TA100, TA1535, TA98 and TA1538) were investigated. LD50-value became smaller with an increase in compound hydrophobicity. The mutagenicities of these compounds TA100 increased in the order: 1-naphthylethyl glycidyl ether less than 2-naphthylethyl glycidyl ether less than benzyl glycidyl ether less than 2-naphthylmethyl glycidyl ether less than 1-naphthylmethyl glycidyl ether less than 9-anthrylmethyl glycidyl ether. 1-Naphthylmethyl and 2-naphthylmethyl glycidyl ethers were mutagenic toward TA1535. In TA98, 1-naphthylmethyl and 9-anthrylmethyl glycidyl ethers showed mutagenic activity and 9-anthrylmethyl glycidyl ether was more mutagenic than 1-naphthylmethyl glycidyl ether. 9-Anthrylmethyl glycidyl ether was also active in TA1538. In the reaction of glycidyl ethers with deoxyguanosine and related compounds, glycidyl ethers attacked at only N-7 of guanine. The alkyl rates of glycidyl ethers toward guanine residues in DNA were determined and the exciplex-formation ability of 7-substituted guanines was studied. The reactivity of glycidyl ethers toward guanine residues in DNA has not provided a sufficient explanation for the variation in mutagenic potencies of glycidyl ethers. (Author abstract)

7. EFFECTS OF P-METHOXYPHENOL AND DIET ON CARCINOGEN-INDUCED NEOPLASIA OF THE MOUSE FORESTOMACH.

Wattenberg LW, Borchert P, Destafney CM, Coccia JB
Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis.
Cancer Res; 43(10):4747-51 1983

Previously, p-methoxyphenol fed in the diet was found to be the most potent inhibitor of benzo(a)pyrene-induced neoplasia of the mouse forestomach of 18 phenols investigated. In the present study, the effects of p-methoxyphenol on the diet-induced carcinogen, beta-propiolactone (BPL), were determined. p-Methoxyphenol administered at 1 or 4 hr prior to BPL fed in the diet markedly inhibited BPL-induced neoplasia of the mouse forestomach. Of 10 phenols tested by p.o. injection, it was the only one that exerted a significant inhibitory activity. Thus far, p-methoxyphenol appears to be an effective inhibitor only when given prior to carcinogen administration. During these studies, it was found that the nature of the carcinogen markedly altered the neoplastic response of the mouse forestomach to BPL but not to benzo(a)pyrene. (Author abstract)

0.004) the relative risk estimated for truck drivers employed at least 10 years was 5.5 (CI = 1.8-17.3). Truck drivers with a history of operating vehicles with diesel engines experienced a significant elevated risk compared to non-truck drivers (relative risk = 11.9; CI = 2.3-61.1), but whether the increased risk observed among truck drivers was attributable to diesel exposure could not be evaluated. Nonsignificant excess risks were also seen for tool and die makers as well as for workers in several other industries and occupations. Employment in the motor vehicle manufacturing industry was associated with no significant excess risk of lower urinary tract cancer (relative risk = 1.1; CI = 0.8-1.5). (Author abstract)

65. SMOKING, OCCUPATION, AND HISTOPATHOLOGY OF LUNG CANCER: A CASE-CONTROL STUDY WITH THE USE OF THE THIRD NATIONAL CANCER SURVEY.

Stayner LT, Wegman DH
Industrywide Studies Branch, National Institute for Occupational Safety and Health, Cincinnati, Ohio.
JNCI; 70(3):421-6 1983

The relationships between occupation, smoking, and the three most common histologic types of lung cancer (squamous cell carcinoma, small-cell carcinoma, and adenocarcinoma) were explored in a case-control study with the use of data collected during the Third National Cancer Survey. The largest histologic group was squamous cell carcinoma (152 cases), followed by adenocarcinoma (50 cases), and small-cell carcinoma (45 cases). The control series was comprised of cancers at all anatomic sites except those believed to be associated with either smoking or occupational exposures. Cigarette smoking was significantly associated with all three histologic types of lung cancer. Overall, the relationship with small-cell carcinoma was strongest (odds ratio = 5.1), whereas those with squamous and adenocarcinoma were approximately equivalent (odds ratio = 3.1). Dose-response relationships were evident for all three histologic types; however, the linear relationship was found to be statistically significant (P less than 0.05) only for squamous and small-cell carcinomas. Squamous cell carcinoma was the type most frequently associated with occupational categories. It was significantly associated (P less than 0.05) with 'blue collar' professions (odds ratio = 2.1). No occupational categories were significantly associated with adenocarcinoma. In addition, no occupational categories were associated with all histologic types of lung cancer combined. This last observation suggested that the sensitivity of epidemiologic studies might not only be increased by use of improved occupational histories but more specifically by consideration of histology in examination of associations between occupation and respiratory cancer. (Author abstract)

66. RESPIRATORY CANCER AND PROFESSIONAL ENVIRONMENT.

Curtes JP
No affiliation given
Arch Mal Prof; 43(8):669-670 1982

Certain studies have shown that 80% of human cancers are linked to environmental factors. For respiratory cancer, it is certain that the most important causal factor is cigarette smoke followed by industrial pollution. Industrial carcinogens include mineral agents and organic agents. Mineral agents which have been seriously implicated in carcinogenesis are As, Be, Cr, Fe, and Ni. Gas and radioactive particles are responsible for pulmonary cancers, and in South Africa, Rn has been responsible for increased rates of pulmonary cancer among miners. Carcinogenic agents include aromatic hydrocarbons and wood

dust which is responsible for cancer of the upper airways. Industrial carcinogenesis should be studied in an urgent manner to determine the nature of carcinogens to which workers are exposed and to determine the relationship of carcinogens and the number of workers exposed to different carcinogens. (no Refs) (In FRE)

67. BRONCHIAL PULMONARY CANCERS AND PROFESSIONAL FACTORS.

Chailleux E
Travail de Service de pneumophthysiologie, Hopital Laennec, CHU de Nantes, 44035 Nantes, France
Arch Mal Prof; 43(8):687-689 1982

It is estimated that 80-85% of lung cancers are caused by tobacco, however, work related factors are also responsible for a large percentage of lung cancers. Latency time depends on the particular carcinogen (8-16 yr for chloromethylethers or ionizing radiation and 40 yr for arsenic). Latency is a factor of the cumulative dose, the host response and the type of target cells. Metallic carcinogens which have been extensively studied include nickel, chromium, arsenic, iron, beryllium and asbestos. Asbestos exposure and cigarette smoking are synergistic, and individuals who encompass both factors are 53.24x more likely to develop lung cancer than nonexposed, nonsmoking individuals. Chemical carcinogens include polycyclic hydrocarbons, chloromethylethers, vinyl chloride, and mustard gas. The only causes of pulmonary bronchial cancer officially recognized in France are ionizing radiation, asbestos, and Fe exposure. (no Refs) (In FRE)

68. EXPERIENCE IN ACTIVE DETECTION OF ONCOLOGICAL DISEASES AT INDUSTRIAL ENTERPRISES IN THE ARMENIAN SSR

Mkrtchian LN, Ambartsumian AM, Magakian AG
Vopr Onkol; 29(3):87-90 1983

A questionnaire-based mass screening was conducted at a number of industrial enterprises in the Armenian SSR. The results were evaluated on the basis of 11,035 comprehensive questionnaires. It was found that instrumental, laboratory, X-ray and morphological examination had to be carried out in 1,116 persons (10.1%). Neoplasms of the most frequent localizations were detected in 19 cases (0.17%). The advantages of premedication with seduxen during mass screening are discussed. (Author abstract) (In RUS)

69. ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN SKIN CARCINOGENESIS. INDICATIONS FOR THERAPY AND PREVENTION

Montemari G, Sturis M, Seccia A
Universita Cattolica del Sacro Cuore, Roma, Facolta di Medicina e Chirurgia.
Minerva Med; 74(13):735-40 1983

The authors review the environmental and occupational factors in cutaneous cancerogenesis, group them according to their characteristics, and in particular distinguish between factors of physical and chemical nature. The authors also discuss the influence of predisposing factors related to the somatic makeup (xeroderma pigmentosum) and to work environment. Particular emphasis is given to precancerous skin and therefore to the importance of a mass screening and an effective health education. The authors illustrate the disorder with their clinical pictures. (Author abstract) (In ITA)

sponses were checked for significant differences and a factor analysis was performed. Three factors were extracted for each group. Now it was possible to observe that the smoking and nonsmoking cancer patients displayed very similar results in factor analysis. In the group of smokers we find some more differences between patients and control persons, also in the group of nonsmokers. (no Refs)

95. EPIDEMIOLOGY AND EARLY DETECTION OF CANCER OF THE ESOPHAGUS.

Sorouri P

900 Hillside Road, Wilmington, DE, 19807

Gastrointestinal Cancer 1. DeCosse JJ and Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

The extraordinarily high incidence of esophageal cancer in Iran provides the data base for a review of the epidemiology and early detection of cancer of the esophagus. Cancer of the esophagus is discussed in relation to incidence, sex, age, and racial factors; etiology; and prevention. (153 Refs)

96. EPIDEMIOLOGY OF GASTRIC CANCER AND ITS PRECURSOR LESIONS.

Correa P

Louisiana State Univ. Medical Center, New Orleans, LA, 70112

Gastrointestinal Cancer 1. DeCosse JJ and Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

Epidemiology of gastric cancer is reviewed with respect to etiology. Topics include geographic distribution, sex ratio, time trends, migrant studies, histopathology, blood groups, socioeconomic class, geochemistry, diet, and pernicious anemia. Historic aspects, histologic characteristics, distribution by sex and age, diet, and nitrate intake are considered in relation to precursor lesions of gastric cancer. (40 Refs)

97. METABOLIC EPIDEMIOLOGY OF LARGE BOWEL CANCER.

Hill MJ

Central Public Health Lab., Colindale Ave., London NW9, England

Gastrointestinal Cancer 1. DeCosse JJ and Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981. 575

The epidemiology of large bowel cancer and predisposing and associated diseases are reviewed. Possible causative agents, evidence for the role of bile acids as co-carcinogens, and metabolic epidemiology vis results of studies of the histopathology of large bowel cancer and the adenoma-carcinoma sequence are considered. Variables examined in relation to the development of large bowel cancer include geography, sex, socioeconomic group, race, religion, population density, time and cultural environment. Predisposing diseases include adenomatosis coli, cancer family syndrome, and colorectal adenoma. Associated diseases include associated cancers, diseases of fiber depletion, and others. Possible causative agents are stress and physical factors, radiation, immunological factors, virological factors, environmental agents, endogenous agents (cholesterol, bile acids, steroid estrogens, tryptophan metabolites, tyrosine metabolism, and N-nitroso compounds), nutrition, and genetic factors. (154 Refs)

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98. FURTHER STUDIES ON SKIN MELANOMAS APPARENTLY DEPENDENT ON FEMALE SEX HORMONES

Lee JA, Storer BE

Sch. Public Health and Community Medicine, Dept. Epidemiology SC 36, Univ. Washington, Seattle, WA, 98195

Int J Epidemiol; 11(2):127-131 1982

In the British Isles the incidences and mortality rates from malignant melanoma of the skin have been shown to be higher in females than in males in the later years of reproductive life. In populations with higher rates for malignant melanoma of skin (Scandinavia, Australasia, etc), and also in Japan, where the rates are low, the ratio of female to male deaths is lower than in the British Isles. However, a similar pattern of age-specific sex ratios (risks for females compared with males peaking at some age in the latter half of reproductive life, and relatively low in middle age) is found in these populations. This 'gynecologic' factor is not an artifact of interactions between age and year of birth effects, and appears to act multiplicatively with other etiologic factors. These findings have implications for studies of the etiology and pathogenesis of malignant melanoma, as well as for the descriptive mathematical modelling of the rates for purposes of environmental legislation. (Author abstract) (22 Refs)

99. SOCIO-ECONOMIC CLASS DIFFERENCES IN CANCER INCIDENCE IN CALI, COLOMBIA.

Cuello C, Correa P, Haenszel W

Dept. Pathology, Faculty Medicine, Universidad del Valle Cali, Cali, Colombia

Int J Cancer; 29(6):637-643 1982

Based on census tract information, cancer incidence rates for three socioeconomic strata of the city of Cali, Colombia, were calculated. Strong negative associations with socioeconomic status were found for cancers of the cervix and stomach. Colon cancer and endocrine-related cancers were positively associated with socioeconomic status, while no such association was found for rectal cancer. Contrary to data from developed countries, all smoking-related cancers were positively associated with socioeconomic class. The role of socio-economic gradients in developing countries is stressed as a basis for etiological research. (Author abstract) (30 Refs)

100. TUBERCULOSIS AND LUNG CANCER RISK IN NONSMOKING WOMEN.

Hinds MW, Cohen HI, Kolonel LN

Epidemiology Program, Cancer Center of Hawaii, Univ. Hawaii, Suite 407B, 1236 Lauhala St., Honolulu, HI, 96813

Am Rev Respir Dis; 125(6):776-778 1982

We ascertained prior pulmonary tuberculosis infection in 211 non-Caucasian female lung cancer patients and 419 sex, race, age, smoking history and birthplace-matched control subjects by searching the Hawaii State Tuberculosis Branch patient records. Among never-smokers we found a significant increase in risk associated with prior tuberculous infection (odds ratio, 8.2; 95% confidence limits = 1.3 to 54.4). No such association was found among smokers. Prior tuberculous infection was identified in only 5.5% of never-smoking lung cancer patients, however, suggesting that this factor is a relatively unimportant contributor to the etiologic aspects of lung cancer in persons who have never smoked. (Author abstract) (26 Refs)

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template for formation of new complementary strands. The timing of the replication process is controlled by a biological-clock mechanism that operates within the nucleus. The bonds between components of the DNA molecule are very sensitive to changes in temperature, to chemicals, and to radiation of various kinds. Any of these agents may change the patterns of bonding in the DNA, resulting in a loss of genetic information coded by the DNA base pairs. Loss of information results in a reduction of the cell's capacity to reproduce itself properly. Cross-linking in the DNA molecule contributes to the process of aging and leads to cell death and ultimately to death of the organism. Cellular repair mechanisms exist to correct errors in replication and alterations produced by agents to which DNA is sensitive. Damage to the DNA can result in carcinogenesis, which involves a loss of control over cellular replication. Examples of carcinogenesis include skin cancer induced by exposure to sunlight, lung cancer induced by asbestos dust, and cancers induced by radiation that penetrates the body. Cocarcinogenesis is essentially a process of chemical catalysis. An understanding of the chemical mechanisms of carcinogenesis provides a basis for prevention and treatment of cancer. (43 Refs) (In GER)

187. ETIOLOGY OF ORAL SQUAMOUS CELL CARCINOMA.

Blainie WH, Rankin KV, Mackenzie IC

Department of Pathology, Baylor College of Dentistry, Dallas, Texas.
J Oral Pathol; 12(1):11-29 1983

The traditional list of etiological factors related to oral squamous cell carcinoma namely, tobacco, alcohol, syphilis, and oral sepsis has been expanded to include iron deficiency, chronic candidosis, and herpes simplex virus. The development of current concepts in these areas is discussed. In evaluating the need for future research, special emphasis is given to the concepts of multifactorial etiology and the role of mutagens. Suggestions for future research are discussed. (Author abstract) (95 Refs)

188. ENVIRONMENTAL CAUSES OF CANCER DEATH.

Greenberg ER, Meier FA

Department of Community and Family Medicine, Dartmouth-Hitchcock Medical Center, Hanover, New Hampshire.

Am J Forensic Med Pathol; 3(4):309-13 1982

People increasingly look to the forensic autopsy as a way of determining whether a particular cancer death was environmentally caused. The forensic pathologist must be diligent pursuing evidence that links potential environmental causes to cancer but must also educate the public providing reassurance that most cancers are not due to industrial pollution. Cigarette smoking and various life-style factors appear to account for more cancers than do man-made environmental contaminants. Assessing the possibility that a cancer death is due to a specific environmental agent requires extensive information. First, one must obtain an accurate history of lifetime occupational and environmental exposures. Second, one must analyze this information in view of epidemiologic data on the cancer risks associated with each exposure. Finally, one should seek to document through the autopsy that exposure to a potentially harmful agent actually occurred. The carefully done forensic autopsy can alert the public to dangerous conditions and can provide individuals a basis for recovery in court for damages due to harmful exposures. (Author abstract)

ENVIRONMENTAL AND OCCUPATIONAL CARCINOGENESIS

189. ENVIRONMENTAL ASPECTS OF RESPIRATORY CANCER: MEDICAL LEGAL UPDATE.

Cordasco EM, Morgat EH, Beere F, Popovici M, Murphy F
Med Trial Tech Q; 29(2):229-37 1982

Keywords (MeSH): Carcinogens, Environmental/*adverse effects; Environmental Exposure; Human; Occupational Diseases/chemically induced; Respiratory Tract Neoplasms/*chemically induced; United States Occupational Safety and Health Administration.

190. THE CLINICAL ILLNESS PROMOTION FACTOR: A THIRD INGREDIENT.

Evans AS

WHO Serum Reference Laboratory, Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, Connecticut.

Yale J Biol Med; 55(3-4):193-9 1982

The interactions between a causative agent and a susceptible host involve a series of responses most of which are subclinical or asymptomatic but a few of which are manifested by clinical illness. The factor(s) which tip the balance are poorly understood in both acute and chronic diseases. It is designated here as the clinical illness promoting factor (CIPF), a third ingredient. Among infected persons some leads have been found as to why clinical illness develops: in tuberculosis genetic susceptibility plays a key role, as shown in twin studies; in EBV infections age at the time of infection, genetic, and psychosocial factors determine both the expression and the severity of illness; in poliomyelitis age, exercise in the incubation period, and genetic background are related to the development of paralysis. In the relationship between viruses and cancer, viruses and chronic diseases, or inanimate pathogens like tobacco and lung cancer, we know very little as to the factors that result in clinical disease among the many who are presumably susceptible and fully exposed. Epidemiologic study is urged to identify this CIPF or 'third ingredient'. (Author abstract)

191. RATES OF MUTANT STRUCTURAL CHROMOSOME REARRANGEMENTS IN HUMAN FETUSES: DATA FROM PRENATAL CYTOGENETIC STUDIES AND ASSOCIATIONS WITH MATERNAL AGE AND PARENTAL MUTAGEN EXPOSURE.

Hook EB, Schreinemachers DM, Willey AM, Cross PK

Bureau of Maternal and Child Health, New York State Department of Health, Albany.

Am J Hum Genet; 35(1):96-109 1983

In 27,225 prenatal cytogenetic studies of amniotic fluid reported to the New York State Chromosome Registry and the United States Interregional Chromosome Register System, there were 61 cases with a structural chromosomal abnormality not known inherited, a rate per 1,000 of 2.24. Of these 33, 1.21 per 1,000 were known de novo and nonmosaic; consequently, the rate of events resulting from germinal mutation is highly likely to be between these two limits. The rates per 1,000 of unbalanced abnormalities were 0.59-1.29; of balanced abnormalities, 0.62-0.96; of balanced Robertsonian translocations, 0.22-0.29; and of unbalanced Robertsonian translocations, 0.07-0.11. The rates of fetuses with supernumerary markers and fragments were unexpectedly high: 0.26-0.70 per 1,000. These abnormalities were associated with increased maternal age (38.0 +/- 5.4 to 38.4 +/- 3.6 compared to 35.6 +/- 4.3 in controls), but even after adjustment for the bias to preferential study of older women, the observed rates of these supernumer-

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cytolytic activity directed against an antigen that was specific for the original tumor cell line. (Author abstract)

146. PRODUCTION OF VACCINE TO DEN-INDUCED CARCINOMAS BY IN VITRO ATTENUATION (MEETING ABSTRACT).

Jamashi RJ, Perkins EH
Bowling Green State University, Bowling Green, OH
Proc Am Assoc Cancer Res; 24:939 1983

The degree of immunogenicity of individual diethylnitrosamine (DEN)-induced forestomach carcinomas in female BALB/c mice was investigated following in vivo and in vitro cultivation. Of five transplantable tumor lines studied (DEN1, DEN3, DEN6, DEN8 and DEN9), DEN1, DEN3, and DEN9 were highly tumorigenic, and exhibited very little immunogenicity as judged by the tumor transplantation assay, WINN neutralization and antibody-binding tests. Two lines (DEN6 and DEN8) showed significantly higher immunogenicity by the same assays. Cultured cell lines established from DEN1, DEN3, DEN6 and DEN9 produced squamous cell carcinomas following in vivo inoculation. DEN6 and DEN9 cell lines lost their tumorigenicity at P5 and P40 in culture. In contrast, DEN1 and DEN3 did not lose tumorigenicity through 30-50 passages. However, the number of cells required to produce tumors increased substantially and their ability to metastasize was lost with increase in in vitro passage. Tumor transplantation studies in normal and in immunosuppressed recipients suggested that the decreased tumorigenicity was immunological. When mice were immunized with cells from an in vitro line, strong immunity resulted against both the in vitro and in vivo parental lines suggesting the presence of same or similar antigenic determinants. The antigen(s) involved were not related to retrovirus antigens, since the cell lines did not show viral protein expression. To exclude other in vitro contaminants, such as heterologous serum antigens, tumor cells used for immunization were passaged in vivo at least once. (no Refs)

EPIDEMIOLOGICAL STUDIES AND PUBLIC HEALTH ISSUES INVOLVING NITROSO COMPOUNDS

147. DIET, NUTRITION, AND CANCER: INTERIM DIETARY GUIDELINES.

Palmer S, Bakshi K
National Academy of Sciences, Washington, D.C.
JNCI; 70(6):1151-70 1983

The Committee on Diet, Nutrition, and Cancer of the National Academy of Sciences recently evaluated the role of diet in carcinogenesis. Both epidemiological and laboratory evidence suggests that a high intake of total fat increases susceptibility to cancer of different sites, particularly the breast and colon. In epidemiological studies frequent consumption of certain fruits and vegetables and in laboratory experiments some components of fruits and vegetables, especially cruciferous vegetables, appear to decrease the incidence of cancers at various sites. In contrast, frequent consumption of salt-cured, salt-pickled, or smoked foods, possibly because they may contain nitrosamines or polycyclic aromatic hydrocarbons, appears to increase the risk of esophageal or stomach cancer. Excessive alcohol consumption among smokers appears to be associated with an elevated risk of cancers of the oral cavity, esophagus,

larynx, and respiratory tract. Interim dietary guidelines to reduce the risk of cancer were proposed in accordance with these conclusions. No definitive conclusions were reached for other dietary factors, including total calories, cholesterol, fiber, and selenium, nor could the quantitative contribution of diet to overall cancer risk be estimated. (Author abstract)

148. NITRATE AND NITRITE CONTENTS IN CUBAN CHEESE OF THE GOUDA TYPE.

Garcia Roca MO, del Pozo E, Izquierdo L, Fontaine M
Cuban National Institute of Hygiene, Havana.
Nahrung; 27(2):125-8 1983

The nitrate and nitrite contents in cheese of the Gouda type, produced by the Milk Complex of Havana, were investigated and compared with those found in 5 types of imported cheese consumed in Cuba. No significant differences were found in the mean value (mean) of NaNO₃, whereas in the mean value (mean) of NaNO₂ differences were found when comparing all cheeses against each other. From these results it is inferred that the consumption of Gouda type cheese does not represent an important contribution to the daily intake of nitrates and nitrites, precursors in the synthesis of cancerogenic N-nitroso compounds. (Author abstract)

149. INHIBITORY EFFECT OF BETEL NUT EXTRACTS ON ENDOGENOUS NITROSATION IN HUMANS.

Stich HF, Ohshima H, Pignatelli B, Michelson J, Bartsch H
Environmental Carcinogenesis Unit, British Columbia Cancer Research Centre, Vancouver, Canada.
JNCI; 70(6):1047-50 1983

Extracts of betel nut (Areca catechu) were tested for their capacity to inhibit the endogenous formation of nitrosamines by measurement of the amount of urinary N-nitroso-L-proline (NPRO) following ingestion of sodium nitrate (300 mg) and L-proline (300 mg) by 2 volunteers. A water extract of the dried nuts, an ether extract containing mainly (+)-catechin and (-)-epicatechin, and a caffeine-precipitated n-butyl alcohol extract containing primarily proanthocyanidins (tannins) strongly reduced the endogenous formation of NPRO. An average of 14.7 and 10.9 micrograms NPRO (8 expts per individual) was excreted in the urine of the 2 volunteers over a 24-hour period following the intake of sodium nitrate and L-proline. The water extract and the proanthocyanidin (tannin)-containing extract, both of which contain the dose equivalent of one-quarter of a nut, reduced the excreted NPRO to background levels, which varied from 0.5 to 3.6 micrograms and from 0.6 to 2.1 micrograms (6 expts) in 24-hour urine samples from the 2 volunteers. These results may exemplify the way in which naturally occurring phenolics, which are ingested daily in relatively large quantities, could affect the endogenous formation of carcinogenic nitrosamines. (Author abstract)

150. ON THE ENDOGENOUS FORMATION OF N-NITROSAMINES IN CIGARETTE SMOKERS (MEETING ABSTRACT).

Hoffmann D, Haley NJ, Brunnemann KD, Wynder EL
American Health Foundation, Valhalla, NY
Proc Am Assoc Cancer Res; 24:241 1983

Age adjusted groups of five cigarette smokers and five non-smokers were placed on a standardized and controlled diet for 12 days. Daily supplements of 300 mg proline were given on days 4, 5 and 6. Supplements of 300 mg proline and 1,000 mg ascorbic acid were given on days 7, 8 and 9. Finally, on days

10, 11 and 12, only 1,000 mg ascorbic acid were given in addition to the standardized diet. Twenty-four hour urine samples were collected in stopping solution on days 3, 6, 9, and 12. Aliquots of these were analyzed for nicotine and cotinine by RIA (radioimmunoassay) and for pH, creatinine, PRO, nitrite and nitrate. For the analysis of N-nitrosoproline (NPRO), an indicator for in vivo N-nitrosation of amines, we modified the method of Ohshima and Bartsch. The results suggest that cigarette smokers can form higher amounts of NPRO in vivo than nonsmokers. This observation cannot be explained only by the depth of inhalation of smoke which is determined by blood analysis for nicotine, cotinine, and COHb. The presentation will include data as to the in vitro formation of nitrosamines from PRO and nicotine in the blood of these smokers. The increased formation of NPRO in cigarette smoke inhalers is inhibited by the addition of ascorbic acid to the diet. These findings and data on the in vivo formation of tobacco-specific N-nitrosamines and on the transnitrosation from NPRO will be presented and discussed. (1 Ref)

151. INHIBITION OF N-NITROSAMINE FORMATION IN BACON BY ALPHA-TOCOPHEROL-COATED SALT SYSTEMS.

Reddy SK
Michigan State University, East Lansing, MI
Diss Abstr Int [B]; 43(9):2846-B 1983

The effects of alpha-tocopherol-coated salt systems on the inhibition of N-nitrosamine formation were investigated in both dry cured and brine cured bacon. In dry cured bacon, approximately a 95% reduction in N-nitrosopyrrolidine (NPYR) levels in the fried bacon was achieved with an ingoing alpha-tocopherol level of 500 mg/kg. NPYR levels in the cook-out fat were reduced approximately 92% using the same level of alpha-tocopherol. Bacon prepared by a small scale commercial operation also contained reduced levels of NPYR when processed with alpha-tocopherol-coated salt, despite the high levels (greater than 100 mg/kg) of residual sodium nitrite in the finished bacon. Alpha-tocopherol also appeared to be more effective as a blocking agent (91% versus 73% inhibition of NPYR) compared to the mixed tocopherols. Brine cured bacon was also manufactured using brines containing alpha-tocopherol-coated salts. In order to achieve greater stability in the brine system, lecithin was also coated on the surface of the salt. Results of the N-nitrosamine analyses indicate a very high degree of inhibition of NPYR formation in both fried bacon (approximately 90%) and the cook-out fat (97-100%) with an ingoing alpha-tocopherol level of 500 mg/kg. Alpha-tocopherol was also effective in minimizing N-nitrosodimethylamine (NDMA) formation in fried bacon. However, there was a wider variation (76-92%) in the percent inhibition obtained for NDMA. Less inhibition of NDMA formation in the cook-out fat was also observed. The possible relationship of unsaturated fatty acids to the formation of N-nitrosamines in bacon was evaluated by swine feeding trials in which pigs were fed regular, alpha-tocopherol-enriched and corn oil-supplemented diets. Fatty acid analyses of the bacon indicated an approximate two fold increase in linoleic acid in bacon made from pigs fed the corn oil-supplemented diet. No obvious effects on the formation of NPYR were observed in bacon manufactured from the pigs. However, bacon made from swine fed the corn oil-supplemented diets contained much higher levels of NDMA (an approximate six-fold increase) than the control bacon. These results may indicate that the high levels of unsaturated fatty acids in bacon adipose tissue may enhance the formation of NDMA in fried bacon. (no Refs)

152. AGRICULTURALLY RELATED CARCINOGENIC RISK (MEETING ABSTRACT).

Bornazsanyi M, Torok G, Pinter A, Sarjan A
National Institute of Hygiene, 1966 Budapest, Hungary
Symposium on Role of Cocarcinogens and Promoters in Human and Experimental Carcinogenesis, May 16-18, 1983, Budapest, Hungary
Hungarian Cancer Society, 1983.

Carcinogenesis is a multistage process where etiological factors can be regarded as complete carcinogens, initiators or promoters. Despite the rather limited number of definitive human carcinogens, the increasing amount of environmental pollutants might fall in one or other categories of carcinogens. Development in chemical industry resulted in chemisation of agriculture which along with the spread of industrial methods might represent real danger for human being. In this paper we give an account about agricultural chemicals which could play a role in the carcinogenic process. The use of the herbicide 1-naphthylamine may be dangerous because of the presence of bladder carcinogen 2-naphthylamine. Important group of agricultural chemicals have alkylating properties like halogenated hydrocarbons (alkanoles, aryl derivatives, alkan halides etc), which are mutagenic and carcinogenic in animals. Some organophosphate pesticides are also widely used and proved to be genotoxic. Pesticides containing secondary, tertiary and quaternary amino groups could be converted to N-nitroso compounds in vitro and in vivo. We were able to demonstrate in vivo nitrosation of carbamate, morpholine, urea, piperazine and guanidine pesticides, of which N-nitroso derivatives caused tumors in experimental animals. This points to the importance of nitrite and nitrate, present in the environment. The above discussed compounds, having definitive effect in short term genotoxicity tests might endanger human population as initiators or complete carcinogens. Non-genotoxic agricultural chemicals include some highly stable, eventually cumulating compounds which either do not induce tumors or increase only the frequency of spontaneous neoplasms. Such group of chemicals is represented mainly by polychlorinated biphenyl pesticides and the TCDD as pesticide contaminant. (no Refs)

153. N-NITROSODIETHANOLAMINE IN ANTIFREEZE.

Ducos P, Maire C, Lissac JC, Gaudin R
Institut National de Recherche et de Securite, Nancy, France.
Environ Res; 31(1):95-9 1983

Carcinogenic N-nitrosodiethanolamine has been found at concentrations varying from 15 to 5700 mg/liter in several leading French brands of antifreeze. Moreover, mixtures of antifreezes which, separately, are innocuous, can form this nitrosamine which appears to arise from interaction of triethanolamine derivatives with sodium nitrite. It is recommended that sodium nitrite be abandoned as an anticorrosion additive. (Author abstract)

154. LONG-TERM RISK OF NEOPLASMS AFTER BILLROTH I AND BILLROTH II RESECTION OF THE STOMACH FOR DUODENAL ULCER (MEETING ABSTRACT).

Gandagai S, Bernardini G, Pistoia MA, Amicucci G, Tuscano D, Masci C, Agnifili A, Negro P
Clinica Chirurgica, L'Aquila, Italy
1 Corso Internazionale de Aggiornamento in Diagnostica e Chirurgia Endoscopica, December 2-4, 1982, Catania, Sicily. Societa Italiana di Endoscopia Digestiva 304 pp., 1982.

Billroth II resections of the stomach seem to have a higher incidence of carcinoma of the gastric stump than Billroth I op-

cytolytic activity directed against an antigen that was specific for the original tumor cell line. (Author abstract)

146. PRODUCTION OF VACCINE TO DEN-INDUCED CARCINOMAS BY IN VITRO ATTENUATION (MEETING ABSTRACT).

Jamasbi RJ, Perkins EH
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ANALYTICAL AND METHODOLOGICAL ASPECTS OF CANCER EPIDEMIOLOGY

54. SUSCEPTIBILITY TO CANCER AND SPONTANEOUS INCIDENCE.

Reif AE

Laboratory of Experimental Cancer Immunotherapy, Boston University School of Medicine, Boston City Hospital, Mass.
Oncology; 40(3):210-7 1983

Susceptibility to cancer implies being easily affected by carcinogen, as well as having an overt spontaneous incidence of cancer. The susceptibility of a population to the development of fatal cancer of a given organ can be represented by a frequency distribution. This distribution depends both upon the genetic susceptibility of the population and upon all environmental carcinogens that have impinged on that population. The method for construction of such a susceptibility distribution has been simplified and applied to experimental data on bone tumor induction with 90Sr in mice, and to bone tumor mortality and prostate cancer mortality in man. The relative susceptibilities of different human organs to the development of fatal tumors can be defined in terms of the spontaneous tumor mortalities. (Author abstract)

55. REPRODUCIBILITY OF A DIET HISTORY QUESTIONNAIRE IN A CASE-CONTROL STUDY OF BREAST CANCER.

Hankin JH, Nomura AM, Lee J, Hirohata T, Kolonel LN
Epidemiology Program, University of Hawaii, Honolulu.
Am J Clin Nutr; 37(6):981-5 1983

The reproducibility of a diet history questionnaire was assessed as part of a case-control breast cancer study in Caucasian and Japanese women in Hawaii. The method was designed to estimate the intakes of total and saturated fat, cholesterol, and animal protein during a usual week before symptoms or diagnosis of disease in cases, and during a usual recent week in controls. Except for the time period of reference, the dietary technique was identical for all cases and controls. A subsample of 61 Japanese women (19 cases and 42 controls) and 56 Caucasian women (23 cases and 33 controls) participated in the dietary reinterview conducted within 3 months of the first interview. The mean difference in intake between the two interviews was small and not statistically significant (p greater than 0.05) for all four nutrient items among Japanese cases and controls and Caucasian cases, whereas the mean difference for all four nutrients was substantial and statistically significant (p less than 0.05) among the Caucasian controls. The intraclass correlation and the product-moment correlation were moderately high for all four nutrient items among Japanese cases and controls and Caucasian cases, but not among Caucasian controls. These findings indicate that the diet history method is reasonably reproducible in three of the four groups of studied subjects. Possible reasons for the poor reproducibility among Caucasian controls are discussed. (Author abstract)

56. GROUPING OCCUPATIONS ACCORDING TO CARCINOGENIC POTENTIAL: OCCUPATION CLUSTERS FROM AN EXPOSURE LINKAGE SYSTEM.

Hsieh CC, Walker AM, Hoor SK
Department of Epidemiology, Harvard School of Public Health, Boston, MA.
Am J Epidemiol; 117(5):575-89 1983

An occupational clustering scheme has been developed from an occupation and exposure linkage system. In this scheme, occupational titles are grouped together hierarchically according to the numbers and degrees of their shared exposures. The use of the clusters obtained from this hierarchy is demonstrated in the analysis of the data from a case-control study of bladder cancer. (Author abstract)

57. EPIDEMIOLOGIC INVESTIGATIONS. CARE IN CONDUCT, CARE IN ANALYSIS, AND CARE IN REPORTING.

Mantel N
Dept. of Mathematics, Statistics and Computer Science, American University, Bethesda, MD.
J Cancer Res Clin Oncol; 105(2):113-6 1983

Keywords (MeSH): Adult; Age Factors; *Epidemiologic Methods; Female; Human; Lung Neoplasms/mortality; Male; Middle Age; Prospective Studies; Research Design; Smoking; Statistics; ;

58. IS THERE A CANCER-PRONE PERSONALITY? (44 REFS)

Wellisch DK, Yager J
Neuropsychiatric Institute, University of California, Los Angeles, CA; 33(3):145-53 1983

Keywords (MeSH): Disease Susceptibility; Epidemiologic Methods; Hormones/physiology; Human; Neoplasms/immunology/occurrence/*psychology; *Personality; Research Design; Review.

GENERAL AND MISCELLANEOUS FACTORS

59. ROLE OF EXOGENOUS AND ENDOGENOUS FACTORS IN THE ETIOLOGY OF HUMAN TUMORS

Turner VS
Arkh Patol; 45(2):3-13 1983

The factors of major importance in the development of human tumors: exogenous chemical carcinogens, endogenous carcinogens, hormones, radiation, immunity disorders, heredity, nutrition, harmful habits are analysed on the basis of epidemiological and experimental evidence. Close interaction of exogenous and endogenous factors in the process of tumor development is demonstrated. Occupational carcinogens affecting at high doses small human contingents are frequently the major etiological cause of tumor development. In the general population exposed to the effect of quite low doses of carcinogens the latter are probably only initiators of neoplastic process completed by specific and nonspecific stimulators of carcinogenesis (cocarcinogens, promoters). The mechanisms of action of modifying factors on carcinogenesis (the effect of carcinogens on endogenous synthesis and metabolism, their interaction with cell macromolecules, tumor growth) are discussed. (Author abstract) (67 Refs) (In RUS)

we have measured the kinetics of removal of this alkylating product from the DNA of human fibroblasts treated with the N-nitroso carcinogen N-ethyl-N-nitrosourea. A very similar rate of elimination from DNA was found in two normal human fibroblast strains (GM730 and 54BR) and in the nonvirus-transformed xeroderma pigmentosum fibroblast strains XP1BI and XP3BR. This is in contrast to the SV40-transformed xeroderma pigmentosum fibroblast strain XP12RO-SV40 which had previously been shown to be defective in its ability to remove O6-ethylguanine from DNA. (Author abstract)

EPIDEMIOLOGICAL STUDIES AND PUBLIC HEALTH ISSUES INVOLVING NITROSO COMPOUNDS

49. BILE ACIDS, BUT NOT NEUTRAL STEROLS, ARE TUMOR PROMOTERS IN THE COLON IN MAN AND IN RODENTS.

Weisburger JH, Reddy BS, Barnes WS, Wynder EL
American Health Foundation, Valhalla, NY.
Environ Health Perspect; 50:101-7 1983

Analysis of the etiologic factors and relevant mechanisms involved in carcinogenesis leads to a classification of agents involved in the carcinogenic process as genotoxic or epigenetic. Their mode of action is distinct, especially with regard to dose-response effects and reversibility. The genotoxic carcinogens for colon cancer are unknown, but mutagenic components found in fried beef and fish are under study. Epigenetic agents as promoting factors play a major role in the development of cancer of the colon. Specific nutritional elements associated with colon cancer risk are high fat diets, high cholesterol intake, and low fiber intake. The role of micronutrients as modulators and inhibitors needs to be explored. Through metabolic studies in diverse populations and in reliable animal models, it is now clear that dietary fat and cholesterol control the total flow of bile acids in lumen and a high-fat, high-cholesterol diet increases the total of bile acids in the gut. Bile acids but not neutral sterols have promoting effects and are related to colon cancer risk although bile acids by themselves do not act as complete carcinogens. The effect of dietary fiber such as cereal bran is to increase stool bulk which dilutes the concentration of bile acids. Reducing the concentration of bile acids either by lower dietary fat and cholesterol or by increasing dietary fiber may effectively lower the risk for colon cancer. (Author abstract)

50. N-NITROSO COMPOUNDS: EVIDENCE FOR THEIR PRESENCE IN AIRBORNE PARTICLES.

Kneip TJ, Dalseg JM, Solomon JJ, Hershman RJ
Institute of Environmental Medicine, New York University Medical Center, New York.
Science; 221(4615):1045-7 1983

Chemical, infrared, and thermal energy analyses have provided evidence for the presence of the N-nitroso functional group in extracts of airborne particles. The total molar N-nitroso concentrations in New York City air are equivalent to the total concentrations of polycyclic aromatic hydrocarbons. Since 90 percent of the N-nitroso compounds that have been tested are carcinogens, the newly discovered but untested materials may represent a significant environmental hazard. (Author abstract)

CHEMICAL CARCINOGENESIS; Nitroso Compounds

51. THE PROBLEM OF NITROSAMINES IN THE RESIDUAL GASES OF AMINE PRODUCTION

Bittersohl G, Heberer H
Z Gesamte Hyg; 29(5):270-1 1983

Keywords (MeSH): Air Pollutants/*analysis; Air Pollutants, Environmental/*analysis; Amines/*chemical synthesis; English Abstract; Gases/analysis; Nitrosamines/*analysis.

REVIEWS INCLUDING NITROSO COMPOUNDS

52. EXPERIMENTAL CARCINOGENESIS OF THE STOMACH AND ITS MODIFIERS

Takahashi M
Dept. of Pathology, National Institute of Hygienic Sciences.
Gan To Kagaku Ryoho; 10(2 Pt 2):421-7 1983

Modifiers of gastric carcinogenesis are reviewed with evidence of experimental results using rats. 1) Physical modifiers: Route of administration, medium (vehicle) of carcinogens, detergents, dosage (concentration), period (frequency) of administration, exposure time, and condition of mucus. Effects of surfactants and presence of a foreign body in the stomach lumen are also samples of physical enhancing factors. 2) Biological modifiers: Species, genetics, sex, hormonal factors, nutrition, and age. Moreover, effect of preexisting ulceration is important. 3) Chemical modifiers: Chemical substances administered prior to, simultaneously with, or following exposure of experimental animals to chemical carcinogens, or promoters of carcinogenesis. Chemical modifiers are: co-initiators, tumor promoters and inhibitors. NaCl having both co-initiator and tumor promoter action on MNNG gastric carcinogenesis is clearly shown in our investigations. (Author abstract) (In JPN)

53. GENETIC FACTORS IN GASTRIC CARCINOGENESIS

Ohgaki H
Biochemistry Division, National Cancer Center Research Institute.
Gan To Kagaku Ryoho; 10(2 Pt 2):428-32 1983

Genetic control of susceptibility of rats to gastro-carcinogenesis by N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) was studied in susceptible ACI strain rats, resistant Buffalo strain rats, and their F1 and F2 offsprings. Rats were given MNNG at a concentration of 83 micrograms/ml in drinking water for 32 weeks and sacrificed on week 72. The incidence of gastric adenocarcinomas in F1 was as low as that in Buffalo rats. The results showed that susceptibility to MNNG was controlled genetically and that the resistance of Buffalo strain rats was autosomal dominant. To clarify the mechanisms which determine susceptibility to MNNG, some biochemical parameters such as pH of gastric juice, glutathione content in the gastric mucosa and the binding of MNNG to DNA, were analysed. No difference was observed between ACI and Buffalo strains in regard to the events leading to the binding of MNNG to DNA. (Author abstract) (In JPN)

observed patterns, and further inquiries into this question, therefore, may be useful. (Author abstract)

95. LUNG CANCER IN NONSMOKERS.

Kabat GC, Wynder EL
Division of Epidemiology, Mahoney Institute for Health Maintenance,
American Health Foundation, New York, New York.
Cancer; 53(5):1214-21 1984

Among 2668 patients with newly diagnosed lung cancer interviewed between 1971 and 1980, 134 cases occurred in 'validated' nonsmokers. The proportion of nonsmokers among all cases was 1.9% (37 of 1919) for men and 13.0% (97 of 749) for women, giving a sex ratio of 1:2.6. Kreyberg Type II (mainly adenocarcinoma) was more common among nonsmoking cases, especially women, than among all lung cancer cases. Comparison of cases with equal numbers of age-, sex-, race-, and hospital-matched nonsmoking controls showed no differences by religion, proportion of foreign-born, marital status, residence (urban/rural), alcohol consumption or Quetelet's index. Male cases tended to have higher proportions of professionals and to be more educated than controls. No differences in occupation or occupational exposure were seen in men. Among women, cases were more likely than controls to have worked in a textile-related job (relative risk = 3.10, 95% confidence interval 1.11-8.64), but the significance of this finding is not clear. Preliminary data on exposure to passive inhalation of tobacco smoke, available for a subset of cases and controls, showed no differences except for more frequent exposure among male cases than controls to sidestream tobacco smoke at work. The need for more complete information on exposure to secondhand tobacco smoke is discussed. (Author abstract)

96. EPIDEMIOLOGY OF CEREBRAL GLIOMAS

Scalzi R
Università degli Studi di Pavia, Servizio di Neuropatologia della Clinica Neurologica 'C. Mondino'.
Minerva Med; 75(21):1259-63 1984

In the present review the results of the main epidemiologic studies on cerebral gliomas are reported. Various characteristics of patients, i.e. endogenous factors including age, sex, familiarity and constitutional factors, and exogenous factors including perinatal and infectious diseases, trauma and geographic and environmental findings, are considered in turn. (Author abstract) (In ITA)

97. STATISTICS AND VARIOUS ASPECTS OF THE EPIDEMIOLOGY OF LYMPHATIC AND HEMATOLOGIC NEOPLASMS (59 REFS)

Lebedev VN
Vopr Onkol; 30(4):82-96 1984

Keywords (MeSH): Adolescence; Adult; Age Factors; Aged; Child; Child, Preschool; Comparative Study; Epidemiologic Methods; Female; Human; Infant; Leukemia/*occurrence; Lymphoma/*occurrence; Male; Middle Age; Review; Sex Factors; USSR.

98. EPIDEMIOLOGY OF CANCER OF THE ESOPHAGUS.

Schottenfeld D
Department of Epidemiology and Preventive Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY.
Semin Oncol; 11(2):92-100 1984

Keywords (MeSH): Adult; Africa; Age Factors; Alcohol Drinking; Asia; Disease Susceptibility; Esophageal Neoplasms/

etiology/mortality/*occurrence; Female; France; Human; Male; Middle Age; Nutrition; Risk; Sex Factors; Smoking; ; United States.

99. EPIDEMIOLOGY OF BREAST CANCER AT KENT GENERAL HOSPITAL.

Ford J Jr
Del Med J; 56(2):67-9 1984

Keywords (MeSH): Adult; Aged; Breast Neoplasms/*occurrence/pathology; Carcinoma, Ductal/occurrence; Carcinoma, Scirrhous/occurrence; Delaware; Female; Human; Middle Age.

100. EPIDEMIOLOGIC ASPECTS OF AN OUTBREAK OF ACQUIRED IMMUNODEFICIENCY IN RHESUS MONKEYS (MACACA MULATTA).

Lerche NW, Henrickson RV, Maul DH, Gardner MB
California Primate Research Center, University of California, Davis.
Lab Anim Sci; 34(2):146-50 1984

Since August 25, 1981, an outbreak of simian acquired immunodeficiency syndrome (SAIDS) has been recognized in a single outdoor corral housing 77 rhesus monkeys (*Macaca mulatta*) over a 16-month period. The etiology of this syndrome is unknown but epidemiologic evidence suggests an infectious agent. Thirty-two cases of SAIDS have been identified (31 female, 1 male), and 27 of these animals have died (case fatality rate = 84%). Three of these deaths occurred among 13 infants born in the corral. All 27 deaths were females. For animals in the original cohort, sex was not a statistically significant risk factor. For animals born in the corral females were at greater risk ($p = 0.0489$; Fisher's Exact Test). SAIDS mortality rates were highest for animals entering the corral at less than 30 months of age (4.4 deaths per 100 monkey months of follow-up) and for animals born into the cage (3.3 deaths per 100 monkey-months of follow-up). The mortality rate was lowest for animals entering the corral at greater than 30 months of age, (0.32 deaths per 100 monkey-months of follow-up). No significant associations were found for the factors weaning history, cage-move history, parentage, generation, and medical history, including history of bite-wound trauma. Nine of the original 64 animals entering the corral on August 25, 1981, were previously associated with a group of 110 rhesus monkeys occupying this same corral from September 1976 to August 1981. Though less dramatic, a similar pattern of morbidity and high mortality was recognized retrospectively in this group. (ABSTRACT TRUNCATED AT 250 WORDS) (Author abstract)

101. EPIDEMIOLOGY OF AIDS

Seale J
Z Hautkr; 59(8):525-8 1984

Keywords (MeSH): Acquired Immunodeficiency Syndrome/*occurrence/transmission; Animal; Blood Transfusion/adverse effects; English Abstract; Female; Haiti; Homosexuality; Human; Kuru/occurrence; Male; New Guinea; Sarcoma, Kaposi's/occurrence; Scrapie/occurrence; Sex Behavior; Sheep; Slow Virus Diseases/occurrence; United States.

who had been exposed to 'high' levels of formaldehyde. There were no trends of increasing mortality with duration of work or interval since first exposure. This result may be a chance finding or reflect the influence of smoking or some other factor. Although a carcinogenic action of formaldehyde seems less likely as an explanation it cannot be excluded. The statistical power of the study to detect various risks of nasal cancer is described. (Author abstract)

45. HUMAN HEALTH EFFECTS OF EXPOSURE TO CADMIUM.

Hallenbeck WH

School of Public Health, University of Illinois at Chicago.

Experientia; 40(2):136-42 1984

The health effects of human exposure to cadmium are discussed with emphasis on intake, absorption, body burden, and excretion; osteomalacia in Japan; hypertension; and proteinuria, emphysema, osteomalacia, and cancer in workers. Elevated blood pressure has not been observed as a result of excessive exposures to cadmium in Japan or the workplace. Renal tubular dysfunction and consequent proteinuria is generally accepted as the main effect following long-term, low-level exposure to cadmium. Studies of workers show that proteinuria may develop after the first year of exposure or many years after the last exposure. Proteinuria and deterioration of renal function may continue even after cessation of exposure. The immediate health significance of low-level proteinuria is still under debate. However, there is evidence that long-term renal tubular dysfunction may lead to abnormalities of calcium metabolism and osteomalacia. The few autopsy and cross-sectional studies of workers do not permit conclusions to be drawn regarding the relationship between cadmium exposure and emphysema. Retrospective and historical-prospective studies are needed to settle this important question. No conclusive evidence has been published regarding cadmium-induced cancer in humans. However, there is sufficient evidence to regard cadmium as a suspect renal and prostate carcinogen. Because of equivocal results and the absence of dose-response relationships, the studies reviewed should be used with caution in making regulatory decisions and low-dose risk assessments. (Author abstract) (62 Refs)

46. FORMALDEHYDE TOXICITY. PART II. REVIEW OF ACUTE AND CHRONIC EFFECTS ON HEALTH.

Solomons K, Cochrane JW

Department of Occupational Medicine, National Centre for Occupational Health, Johannesburg.

S Afr Med J; 66(3):103-6 1984

Inhaled formaldehyde has acute effects on the respiratory tract, central nervous system, skin and eyes and also chronic effects on the respiratory tract, particularly on pulmonary function. Formaldehyde has also been associated with adverse reproductive and mutagenic effects, and there is evidence of carcinogenic effects from two important animal studies. Some data, largely indirect, suggest a carcinogenic risk for man. The reactions of some international scientific bodies to the accumulated data are noted, and steps taken by a number of countries to control formaldehyde exposure in the workplace and other environments are discussed. (Author abstract) (51 Refs)

47. AN EVALUATION OF THE ASSOCIATIONS OF LEUKEMIA AND RUBBER INDUSTRY SOLVENT EXPOSURES.

Checkoway H, Wilcosky T, Wolf P, Tyroler H

Occupational Health Studies Group, University of North Carolina, Chapel Hill.

Am J Ind Med; 5(3):239-49 1984

Excessive leukemia mortality has appeared consistently in epidemiological studies of British and U.S. rubber industry workers. Attempts to identify causative factors have focused on exposure to benzene and other solvents. Interpretations of findings from these studies have often been influenced by expectations of a benzene/nonlymphocytic leukemia association, seen from previous work in other settings. However, data from the rubber industry studies have not been consistent with this expectation, as lymphocytic and nonlymphocytic leukemia have shown similar mortality excesses. Data from a small case-control study of lymphocytic leukemia are presented to illustrate an approach that considers multiple solvent exposures. The associations with lymphocytic leukemia risk observed for a number of solvents, most notably carbon tetrachloride and carbon disulfide, were stronger than those detected for benzene. (Author abstract)

48. DOES AGENT ORANGE CAUSE BIRTH DEFECTS?

Friedman JM

Department of Obstetrics and Gynecology, University of Texas Health Science Center, Southwestern Medical School, Dallas.

Teratology; 29(2):193-221 1984

Large quantities of the defoliant, Agent Orange, were sprayed in Vietnam during the war. Agent Orange was composed of two herbicides: 2,4-D and 2,4,5-T, the latter contaminated by small amounts of a highly toxic dioxin (TCDD). The constituents of Agent Orange are capable of producing gene mutations and chromosomal aberrations, at least in some experimental circumstances. TCDD and 2,4,5-T are teratogenic in mice and perhaps in other mammals, but the teratogenicity of these chemicals has not been convincingly demonstrated in humans. There is currently no scientific evidence which indicates that men who were previously exposed to Agent Orange are at increased risk of having children with birth defects, but available data are inadequate to assess this possibility critically. (Author abstract) (105 Refs)

49. A REVIEW OF WORLD LITERATURE FINDS IRON OXIDES NONCARCINOGENIC.

Stokinger HE

Am Ind Hyg Assoc J; 45(2):127-33 1984

Iron oxide appeared in the first list of 154 Threshold Limit Values adopted by the American Conference of Governmental Industrial Hygienists at its April 1949 annual meeting. It was set to control dust and fume at the recommended value of 15 mg/M3, at the time, the limit for an inert or 'nuisance' dust, and was based on studies of welders made earlier by the U.S. Dept. of Labor and by Drinker and Nelson. By 1964, the TLV was tentatively reduced to 10 mg/M3 after a considerable body of literature had accumulated not only on the health experience of welders, but of other occupations involving iron oxides as well. As a group, these studies indicated that 15 mg/M3 permitted too great accumulations of iron pigmentation in the lung whose chronic retention effects were not known with certainty. Also, an occasional report of cancer of the lungs appeared particularly among British hematite miners, although

tigated, most of them handling glass fibers. Several thousands of this workforce had a duration of exposure of 20 years or more and a latency time of 30 years or more. No case of mesothelioma was found. A most of the identified cases of pneumoconiosis could be attached to a prior or a concomitant exposure to silica if the occupational exposure was carefully examined. At the recent time there is no wellfounded suspicion that pneumoconiosis is caused by the exposure in the MMF-industries. A few authors supposed, that unspecific structural changes of the lung as occurring also in a greater amount in dependency of smoking habits and age are found more frequently among the employees of this industry than among the common population. Neither the workers with such unspecific structural changes of the lung nor the other members of the workforces had prejudices of lung function. At present time a risk due to MMF to get sick with cancer of the bronchopulmonic system, especially with lung cancer can neither be proved nor be excluded. The epidemiological studies carried out until now were not capable to point out a possibly existing risk in such a order of magnitude. It is uncertain if it will be feasible to prove such a risk by using more subtilized methods. This depends at one side on the possibility of clearing up and registering the confounding risk factors. On the other side it must be considered, that the exposure with fibrous dusts even in the old MMF-factories was very much lower than the exposure in the asbestos-industry. It is indispensable to take into account the most important confounding risk factors (smoking habits, preexposure and concomitant exposure with dangerous working materials) in further epidemiological investigations. (Author abstract) (41 Refs) (In GER)

56. OCCUPATIONAL EXPOSURES AS RISK INDICATOR OF MALE BLADDER CARCINOMA IN A PREDOMINANTLY RURAL AREA.

Mommsen S, Aagard J
Department of Oncology and Radiotherapy, University of Aarhus, Denmark.
Acta Radiol [Oncol]; 23(2-3):147-52 1984

A case-control study was performed on 212 bladder carcinoma patients (165 men and 47 women) and 259 control persons (165 men and 94 women) matched according to age and geographical area. Bivariate associations among the males revealed an increased relative risk (RR) of developing bladder carcinoma associated with occupational exposure to oil or gasoline, chemical materials, kerosene or asphalt. A significantly increased RR of developing bladder carcinoma was associated with blacksmiths and mechanics. A logistic regression analysis did not reveal an independent statistical effect of this parameter. Among the occupational factors, exposure to oil or gasoline was the most informative aetiologic determinant. (Author abstract)

57. WELDING AND CANCER OF THE LARYNX: A CASE-CONTROL STUDY.

Olsen J, Sabroe S, Lajer M
Department of Social Medicine, University of Odense.
Eur J Cancer Clin Oncol; 20(5):639-43 1984

The purpose of the study was to examine the occupational history of laryngeal cancer patients, and especially their exposure to welding. The investigation was conducted as a case-control study where all newly diagnosed patients less than 75 yr of age with cancer of the larynx in Denmark during March 1980 to March 1982 were selected as cases. For each case, four age- and sex-matched controls were identified from the municipal person register in which the case was listed. Data were col-

lected partly by means of questionnaires and partly by abstracting information from the medical records of cases. Workers exposed to welding fumes had a slightly increased risk of cancer of the larynx, most predominantly of cancer of the subglottic area. (Author abstract)

58. LUNG CANCER MORTALITY IN A COHORT OF ENGLISH FOUNDRY WORKERS.

Fletcher AC, Ades A
Department of Environmental and Occupational Health, University of Aston in Birmingham, United Kingdom.
Scand J Work Environ Health; 10(1):7-16 1984

A cohort of males who started work between 1946 and 1965 inclusive in nine English steel foundries and who worked in these foundries at least one year has been followed prospectively until 1978. Mortality from lung cancer was significantly raised among workers employed in the foundry and fettling shop areas (standardized mortality ratios 142 and 173, respectively). Most occupational categories in these two areas had more lung cancer deaths than expected, but the standardized mortality ratios were the largest for the furnace bricklayers, fettlers, and heat treatment furnacemen. There was some evidence of risk increasing with length of employment. There were marked differences in the standardized mortality ratio for lung cancer between study foundries. By year of entry the lung cancer risk was fairly constant, in contrast to the improvement in mortality from diseases of the respiratory system over the same period. (Author abstract)

59. RESPIRATORY IMPAIRMENT IN COKE OVEN WORKERS: RELATIONSHIP TO WORK EXPOSURE AND BRONCHIAL INFLAMMATION DETECTED BY SPUTUM CYTOLOGY.

Madison R, Affit AA, Mittman C
Occupational Health Section, City of Hope National Medical Center, Duarte, California.
J Chronic Dis; 37(3):167-76 1984

Coke oven workers are at excess risk of developing lung cancer and may be at risk for chronic obstructive lung disease (COLD). We have studied 3799 male workers to assess the relationship between the two diseases. Repeated lung function and sputum cytology tests were obtained over a 3-year period. Sputum samples were assessed using standardized methods; in addition to metaplastic and neoplastic changes, we reproducibly assessed the presence and extent of acute and chronic inflammatory changes. Spirometric flow rates (FEV1) were significantly reduced in workers most exposed to coke oven emissions, particularly in those with excessive inflammatory cells and regular metaplasia in sputum. The presence of reactive bronchial epithelial cells and metaplasia were potent predictors of an abnormal FEV1/FVC. Studies like these may offer a means to investigate the relationship between COLD and lung cancer. Such changes in sputum may identify individuals at risk of developing both diseases. (Author abstract)

60. APPLICATION OF URINE MUTAGENICITY TO MONITOR COAL LIQUEFACTION WORKERS.

Recio L, Enoch HG, Hannan MA, Hill RH
Graduate Center for Toxicology, University of Kentucky, Lexington.
Mutat Res; 136(3):201-7 1984

The Salmonella/microsomal assay was used to monitor workers' urine for mutagenicity as a potential indicator of human exposure to mutagens/carcinogens. Urine samples from

57 workers at a coal liquefaction pilot plant in Catlettsburg, Kentucky, were assayed for mutagenicity during work periods. Urine samples were collected twice during plant operations and once when the individuals were away from the plant for at least 48 h. In 7 individual smokers (5 operator/maintenance workers and 2 administrative staff workers) there was an indication of enhanced urine mutagenicity during work periods. Urine mutagenicity of nonsmokers from the pilot plant was significantly higher than that of an additional control group of nonsmokers from Lexington, Kentucky. While cigarette smoking was the major factor affecting urine mutagenicity, no significant mutagenicity that could be directly attributed to the pilot plant workers' environment was evident. (Author abstract)

61. CANCER MORTALITY PATTERNS BY WORK CATEGORY IN THREE TEXAS OIL REFINERIES.

Thomas TL, Waxweiler RJ, Crandall MS, White DW, Moure-Eraso R, Fraumeni JF Jr
Occupational Studies Section, National Cancer Institute, Bethesda, Maryland.
Am J Ind Med; 6(1):3-16 1984

A previous proportionate mortality ratio analysis revealed elevated mortality from brain tumors, stomach cancer, leukemia, and other cancers among OCAW members employed in three Texas oil refineries. In order to evaluate these findings, complete work histories of cases and a matched set of controls who died from other causes of death were obtained from company personnel records. Work histories were summarized by classifying each job title and department entry into one of several broad work categories of refinery unit operations. A worker was considered 'exposed' to a work category if he was known to have worked at least 1 day in the category 15 or more years prior to his death. Maximum likelihood estimates of the relative risk for brain tumor, stomach cancer, and leukemia were calculated by work category using a procedure for matched case-control data. No strong associations for brain tumor risk were seen with any work categories. A slight association for leukemia was seen among workers in the Treating category, which included unit operations that reduce the level of aromatic and sulfur constituents of petroleum products and combine them with additives to improve their quality. Stomach cancer risk was elevated among maintenance workers and workers exposed to lubricating oils and paraffin wax processing. (Author abstract)

62. RISK OF LUNG CANCER IN WORKERS BELONGING TO THE OCCUPATIONAL GROUP OF MINING AND STONE PROCESSING

Vutuc C
Hygiene-Institut der Universität Wien.
Zentralbl Bakteriol Mikrobiol Hyg [B]; 177(3-4):183-7 1983

Out of 1580 male lung cancer patients and 3160 controls (data collected in a nationwide study) 177 patients and 197 controls belonged to the occupation 'mining and processing of stone' (asbestos, metals and coal excluded). 164 (92.6%) patients had a Kreyberg I tumor, 13 patients a Kreyberg II tumor. There are significant more smokers among patients (98.9%), all patients with a K I tumor were smokers, compared to the controls (82.2%). Patients had a significant longer smoking career (40.9 years) and a higher tar exposure (TE = 2544) compared to the controls (36.2 years, TE = 2223). Lung cancer risk (adj. for age, years of occupation, TE) of smokers belonging to occupation 'stone' compared to smokers belonging to group 'white collar' (no occupational exposure in

their anamnesis) was $R = 2.0a$. Significantly higher risks (adj. for age, TE) were in relation to years of occupation: less than 10 years: $R = 2.2a$, 11-20 years: $R = 2.7a$, 21-30 years: $R = 2.6a$. a P less than 1%; b P less than 5%. (Author abstract) (In GER)

63. CANCER OF THE BLADDER OCCURRING IN OCCUPATIONAL DYE USERS: REPORT OF TWO CASES

Ando M, Takeda H, Mizuo T, Yokokawa M, Ushiyama T
Department of Urology, Tokyo Rosai Hospital.
Hinyokika Kyo; 30(2):223-8 1984

Two cases of occupational dye users were found to have bladder tumors. Case 1 was a 32-year-old male, who had worked at the Yuzen process for the last 7 years. Multiple papillary tumors were seen on the whole wall of the bladder endoscopically and total cysto-urethrectomy and ileal conduit were performed. The pathological examination of the bladder tumors revealed non-invasive transitional cell carcinoma grade I-II. His post-operative course has been uneventful without any signs of tumor recurrence for 31 months. Case 2 was a 46-year-old male, who had worked at the throwing stained silk for the last 28 years. He suffered from severe hematuria for six months. A big egg-sized nonpapillary tumor on the posterior wall of the bladder was found and bilateral cutaneous-ureterostomy was performed but severe gross hematuria remained. Total cysto-urethrectomy was performed but the patient died of progressive disease 5 months later. The bladder tumor was a grade III invasive transitional cell carcinoma. The fact that process workers in the dye manufacturing industry have a high risk of bladder cancer has been well known and mass screening examination on them has been systematically performed. Though there is a higher relative risk of bladder cancer in occupational dye users, systematic screening examination has not been done. We emphasize the necessity for establishing systematic mass screening examination of occupational dye users for the early diagnosis of bladder cancer. (Author abstract) (In JPN)

OCCUPATIONAL FACTORS: GENERAL

64. THE BIO-SOCIAL ELEMENTS OF RISK IN THE INVASIVE CERVICAL CANCER INCIDENCE AMONG A STATIONARY AND MIGRATORY WOMAN POPULATION. A CASE-CONTROL STUDY.

Zema B
Institute of Oncology, Cancer Epidemiology Unit, Gliwice, Poland.
Neoplasma; 31(1):119-27 1984

The incidence risk of invasive cervical cancer has been analyzed in two groups of women--autochthones and migrants--and the higher risk-rate has been proved for the latter. The essential interdependence between the incidence risk of invasive cervical cancer and the danger of industrial dusts and gases influence have been proved for both fractions of women. The higher incidence risk of invasive cervical cancer has been observed among those who had suffered from lithiasis, diabetes, arterial hypertension before, among those who while undergoing the cancer treatment might have also been operated on reproductive organs because of myoma or erosion, or had suffered from syphilis (this has been observed only in relation to the autochthones' population). (Author abstract)

77. ANALYSIS OF THE PREVALENCE OF HEREDITARY ADENOMATOSIS OF THE GASTROINTESTINAL TRACT AMONG THE POPULATION OF MOSCOW

Tatishvili GG, Nikitin AM, Al'tshuler BA
Genetika (Moskva); 20(5):857-63 1984

The prevalence of hereditary autosomal dominant gastrointestinal adenomatosis in the Moscow population was estimated on the basis of elaboration of an indirect method. This estimate was found to be 1:48000. The prevalence observed is discussed in terms of ascertainment problems and peculiarities of the method of calculation proposed. (Author abstract) (In RUS)

78. TRENDS IN THE DISTRIBUTION OF STOMACH CANCER AND CANCER OF THE LARGE INTESTINE AMONG THE POPULATION

Tikhonova NA, Simkina ES, Kozlova EV, Zaseev VK
Vopr Onkol; 30(2):45-51 1984

An inverse correlation in stomach and large bowel cancer distribution was established as a result of an evaluation of cancer morbidity statistics for the City of Moscow in 1965-1980. The structure of gastrointestinal neoplasms in the next five years is likely to undergo changes in female population in which large bowel cancer is leading at present. (Author abstract) (In RUS)

79. SOCIAL FACTORS, DIET AND BREAST CANCER IN A NORTHERN ITALIAN POPULATION.

Talamini R, La Vecchia C, Decarli A, Franceschi S, Grattoni E, Gigoletto E, Liberati A, Tognoni G
Laboratory of Clinical Pharmacology, Istituto di Ricerche Farmacologiche 'Mario Negri', Milan, Italy.
Br J Cancer; 49(6):723-9 1984

The relation of breast cancer to social and dietary variables was evaluated in a case-control study of 368 women with breast cancer admitted to the General Hospital of Pordenone (a town in the eastern side of Northern Italy) and 373 age-matched controls. Occupation was related to the risk of breast cancer, housewives and non-manual workers (teachers and other professionals, clerical workers, etc.) showing relative risks of 1.7 and 2.4 respectively when compared to women occupied in agriculture. The role of education was apparently less important, and not statistically significant. The risk was higher in women who were obese, the trend of increasing risk with increasing body mass index being confined to post-menopausal women. When indicators of dietary fat intake were analysed, a significantly increased risk was found with more frequent consumption of milk and dairy products but the risk estimates were only slightly above unity with reference to meat consumption. Women who drank alcoholic beverages showed a relative risk of 2.5 compared to women who had never drunk, when allowance was made for all identified potential confounding factors. The association between alcohol and breast cancer was not explained by the other dietary variables considered, and the risk estimates were higher for women who drank more wine, or more than one type of alcoholic beverage. Thus, the findings of the present study give evidence in favour of the hypothesis that alcohol consumption is related to the risk of breast cancer. (Author abstract)

80. BIOSOCIAL CORRELATES OF COLORECTAL CANCER IN GREECE.

Papadimitriou C, Day N, Tzonou A, Gerovassilis F, Manousos O, Tri-chopoulos D
Department of Gastroenterology, Evangelismos Hospital, Athens, Greece.
Int J Epidemiol; 13(2):155-9 1984

One hundred consecutive patients with histologically confirmed colorectal cancer and an equal number of age- and sex-matched orthopaedic patients as hospital controls were interviewed about demographic, socioeconomic, biometric and medical variables. Cholecystectomy was significantly more frequent among cases than controls, but there was no side-predilection of the post-cholecystectomy tumours. The frequency of bowel evacuation was significantly higher among cases, particularly those with rectal cancer, an observation which appears contradictory to the 'prolonged bowel transit time-high colorectal cancer risk' hypothesis. No significant differences were found between cases and controls with respect to socioeconomic status, height and weight, smoking habits, use of laxatives and (for females) parity, age at first pregnancy, and age at menopause; however, cases appeared to be younger at menarche. (Author abstract)

81. INCIDENCE OF LUNG CANCER IN FIVE TOWNS IN ISRAEL, 1960-74.

Epstein LM, Katz L, Tamir A, Rishpon S
Department of Family and Community Health, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa.
Isr J Med Sci; 20(1):27-32 1984

Age-standardized incidence rates of lung cancer, based on data from the Israel Cancer Registry, were calculated in five urban areas in Israel during three 5-year periods: 1960-64, 1965-69 and 1970-74. The rates in these towns and during the different periods were compared. For both sexes the incidence was lowest in Jerusalem, the city with the lowest air pollution. The incidence rate of lung cancer in males during the entire period reviewed fell in all towns except for Tel Aviv, where it rose. Cancers of the urinary bladder and of the pancreas did not display these trends. Possible explanations for the differences are discussed. (Author abstract)

82. CARCINOMA OF THE PROSTATE IN ISRAEL: SOME EPIDEMIOLOGICAL AND THERAPEUTIC CONSIDERATIONS.

Servadio C, Mukamel E, Kahan E
Department of Urology, Beilinson Medical Center, Sackler School of Medicine, Tel Aviv University, Israel.
Prostate; 5(4):375-82 1984

Analysis of the different rate of prostatic cancer in Israel among Jews from various countries of origin reveals some very interesting and marked varieties in incidence, which are studied more closely now. Aggressive, combined treatment for the invasive cases of prostatic cancer has been used since 1975. This was based on orchiectomy, DES, and chemotherapy for the stage D2 disease, and on radiotherapy and hormonal therapy for the stage C, and possibly also the stage D1 disease. Results so far have been very encouraging indeed, and with considerably better results than obtained with the individual, more conventional forms of therapy. Five-year survival in the stage D2 disease has been 63.5%, and 87.6% in the stage C (+D1?) disease. It appears that this approach is more justified, certainly in the advanced stages of this disease. (Author abstract)

cancer was 2.1 and the occupational etiologic fraction was 0.33 (95% confidence interval 0.19-0.47). The tobacco etiologic fraction was 0.81, while the two exposures together accounted for 89% of the total burden of incident cases. If 33% of all male lung cancers were of occupational aetiology, then this alone would represent 5% of all cancer deaths. (Author abstract)

64. MYELOPROLIFERATIVE AND LYMPHOPROLIFERATIVE DISORDERS IN TASMANIA, 1972-80: OCCUPATIONAL AND FAMILIAL ASPECTS.

Giles GG, Lickiss JN, Baikie MJ, Lowenthal RM, Pantoni J
Department of Community Health, University of Tasmania Clinical School, Australia.
JNCI; 72(6):1233-40 1984

All cases in a population-based series of myeloproliferative and lymphoproliferative (LP) disorders diagnosed in usual residents of Tasmania between 1972 and 1980 were asked for occupational histories and the occurrence of similar diseases in their close relatives. Occupational risks were observed for males who had farmed, mined, or worked in foundries and for women who had farmed or had been hairdressers. For individual diagnoses, the risk to farmers was seen to vary with age at diagnosis, sex, and region. With regard to familial risks, the LP and MP groups seemed to breed true, relatives being affected with a disorder from the other group not more often than would be expected by chance. The risks were of two kinds: Those to siblings and that between parent and child, particularly between mother and son. Occupational risks for the familial cases were limited to farming particularly in males diagnosed at 65 years of age or older. Females possessed elevated risks for the LP group only, and their highest relative risk was for those diagnosed before age 65. This evidence suggests that familial clustering of these disorders partly may be due to common environmental exposures in males from rural kindreds. (Author abstract)

65. USE OF JOB-EXPOSURE MATRIX IN AN OCCUPATIONAL ANALYSIS OF LUNG AND BLADDER CANCERS ON THE BASIS OF DEATH CERTIFICATES.

Coggon D, Pannett B, Acheson ED
Environmental Epidemiology Unit, Medical Research Council, University of Southampton, England.
JNCI; 72(1):61-5 1984

A job-exposure matrix has been applied in a case-control study of lung and bladder cancer on the basis of occupational information abstracted from British death certificates. The expected association between lung cancer and jobs entailing exposure to asbestos was clearly demonstrated (relative risk, 1.5; 95% confidence interval, 1.2-1.9). The effects of three other known industrial carcinogens were not apparent, and reasons for this were discussed. Also included in the matrix were five substances whose carcinogenicity in humans has not been established. Formaldehyde, diesel fumes, and cutting oils were all associated with carcinoma of the bronchus, but the absence of a risk in 'high-exposure' occupations was against a causal relationship. Bladder cancer was more common in jobs involving high exposure to printing inks (relative risk, 5.0; 95% confidence interval, 1.0-25.8) and cutting oils (relative risk, 1.5; 95% confidence interval, 0.8-2.8). Use of the job-exposure matrix added considerably to the conventional analysis of cancer risk in individual occupational categories. (Author abstract)

ENVIRONMENTAL AND OCCUPATIONAL CARCINOGENESIS

66. A CASE-CONTROL STUDY OF CANCERS OF THE NASAL CAVITY AND PARANASAL SINUSES.

Brinton LA, Blot WJ, Becker JA, Winn DM, Browder JP, Farmer JC Jr, Fraumeni JF Jr
Environmental Epidemiology Branch, National Cancer Institute, Bethesda, MD.
Am J Epidemiol; 119(6):896-906 1984

To examine occupation, smoking, and other risk factors for nasal cancer, a case-control study was conducted among 160 patients, who were admitted to four hospitals in North Carolina and Virginia between 1970 and 1980, and 290 controls. Employment in the furniture industry was not associated with squamous cell tumors, but such employment increased the risk of nasal adenocarcinoma by fivefold. In addition, approximately threefold excess risks of adenocarcinoma were observed for those employed in other industries involving possible exposure to wood dust. Elevated risks among males were also associated with occupational exposures to chromates (relative risk (RR) = 5.1) and chemicals (RR = 2.7). Among females, an excess risk was associated with employment in the textile industry, particularly for jobs involving dust exposure (RR = 2.3). Although there was no evidence that alcohol consumption affected risk, heavy cigarette smokers were at a two- to threefold excess risk (predominantly for squamous cell tumors); in addition, there was evidence that there was an elevated risk associated with the use of snuff. Elevated risks were also associated with histories of nasal polyps (RR = 8.3), recurrent nose bleeds (RR = 2.0), and sinus trouble (RR = 2.7). These findings provide leads for further studies, and underscore the importance of distinguishing between histologic types. (Author abstract)

67. MORTALITY STUDY OF BRITISH PATHOLOGISTS 1974-80.

Harrington JM, Oakes D
Institute of Occupational Health, University of Birmingham, UK.
Br J Ind Med; 41(2):188-91 1984

Membership lists of the Royal College of Pathologists from 1974 to 1980 were used to establish a population of 2307 men and 413 women. During the period of study 126 of these pathologists died and death certificates were obtained for 121. The standardised mortality ratios (SMR) for all causes in men were 56 and in women 99. Deaths from accidents, poisoning, violence, and especially suicide, were noted to be in excess of that expected from the general population but similar to that for medical practitioners. Drug overdose was the cause of each suicide. Excess deaths from lymphatic and haemopoietic neoplasms noted in a previous study were not present but an excess of brain tumours was found. Including 1981 data thus far collected, deaths from brain tumour were apparently in excess (observed 6, expected less than 2.0, p less than 0.02). Possible aetiological hypotheses include previous exposure to organic solvents or tuberculosis infection. In view of the pathologists' exposure to formaldehyde it is interesting to note that no nasal or nasal sinus tumours were reported and the SMR for lung cancer was 41. (Author abstract)

68. ADMINISTRATION OF ANTINEOPLASTIC AGENTS: A PRACTICE WHICH CARRIES A PROFESSIONAL RISK

Zaccara A
Riv Inferm; 2(3):198-201 1983

Keywords (MeSH): Antineoplastic Agents/*adverse effects; Human; Occupational Diseases/*chemically induced; Risk.

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men age 15-24 and 25-34 experienced biphasic mortality trends, with a rise peaking in 1971 and then a fall. (3) The mortality ratios, non-white to white men, age 25-34 and 35-44, were far higher than those of other age groups. (4) The mortality ratios, non-white males to females, increased steadily for all age groups, and those of age groups 15-24 and 25-34 turned up sharply. Selected causes of death (1960-1977) were reviewed to uncover reasons for the unfavorable mortality trends among males. The following causes contributed to rising mortality among males: (a) accidents, suicide, and homicide for white and non-white teenagers and young adults, age 15-24, 25-34 and 35-44; (b) suicide and homicide for non-white men age 45-54; (c) cirrhosis of the liver for white men age 35-44 and for non-white 25-34, 35-44 and 45-54; (d) malignant neoplasms for white men age 35-44 and for non-white age 45-54. (Author abstract)

87. CANCER MORTALITY AMONG PUERTO RICAN-BORN RESIDENTS IN NEW YORK CITY.

Rosenwalke I
University of Pennsylvania, Population Studies Center, Philadelphia.
Am J Epidemiol; 119(2):177-85 1984

More than half the 800,000 Puerto Rican migrants living in the United States resided in New York City in 1970. Mortality statistics from 1969-1971 indicate that Puerto Rican natives in the metropolis have a standardized mortality ratio for cancer which is 77% of that of non-Puerto Rican white males and 81% of that of non-Puerto Rican white females. The age-adjusted death rates of the Puerto Rican-born residing in New York City for cancers of the lung, prostate, bladder, ovary, and rectum are low, ranging from 43-70% of those of non-Puerto Rican whites; rates for breast cancer and colon cancer are somewhat lower relative to those for non-Puerto Rican whites. As is true for Puerto Ricans on the island, migrants to New York City have excessive levels of cancer of the cervix and esophagus (each roughly three times that of non-Puerto Rican whites) and cancer of the stomach (almost twice that of non-Puerto Rican whites). (Author abstract)

88. MORTALITY DIFFERENTIAL FOR CANCER BASED ON SOCIAL CLASS: THE METROPOLITAN REGION OF MONTREAL, 1971

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Soc Sci Med; 18(1):73-81 1984

Cancer mortality rates vary from area to area. Part of this variation is due to socio-economic characteristics of the area and part to other factors including the availability of health services. Three social indicators associated with cancer mortality are used to estimate variations between low and high census sectors within the metropolitan region of Montreal. The components of socio-economic status which have been used are revenue (median family income), education (college and university level) and occupation (higher status profession). For each of the three zones of the metropolitan area - the city of Montreal, the island of Montreal not including the city of Montreal, the north and south shores of the metropolitan area - twenty-five census sectors have been chosen which have higher or lower positions for each of the socio-economic components. For each group standardized death rates were evaluated for each type of cancer and the Poisson test was applied to judge whether the differences between the projected rate and the observed rate were significant. The results indicate a strong indirect relation between the standardized mortality rates and the socio-economic status in the central city. In the

case of lung cancer, the spatial distribution showed district gradients of occurrence between the central-city and the suburbs. (Author abstract) (In FRE)

89. CANCER MORTALITY AMONG IMMIGRANT POPULATIONS IN ONTARIO, 1969 THROUGH 1973.

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Can Med Assoc J; 130(4):399-405 1984

Ontario is home to a sizeable, recently established immigrant population whose cancer mortality has until now remained unexamined. The province's six largest immigrant groups (British, Italian, German, Dutch, Polish and Soviet) were investigated to compare their cancer mortality experience with that prevailing in Ontario and in their countries of birth for the period 1969 through 1973. Standardized mortality ratios (SMRs) were computed from data from Statistics Canada and the World Health Organization (for 1971) for five sites of cancer. The rates of death from stomach cancer were significantly higher for the immigrant groups (except the Germans) than for the Canadian-born (SMRs 158.6 to 256.1) and were significantly lower for the immigrants (except the Dutch) than for the populations of their countries of birth (SMRs 26.5 to 72.9). The rates of death from colorectal cancer and cancer of the breast tended to be lower among the immigrants. Most male immigrants had high rates of death from lung cancer relative to the Canadian-born, whereas their female counterparts had relatively low rates. For most of the immigrant groups the rates of death from prostate cancer closely resembled those prevailing in the country of birth. Displacement of cancer mortality experience towards that in Ontario was most evident for Polish immigrants. It may have been too soon to see trends among the more recent immigrants (Italian, German and Dutch), who, for the most part, had not yet reached the age of highest cancer risk. Ontario should provide a valuable resource for further studies of lifestyle and environmental determinants of cancer. (Author abstract)

OTHER EPIDEMIOLOGICAL FINDINGS

90. EPIDEMIOLOGY OF KIDNEY CANCER.

Dayal H, Kisman J
Statistical Laboratory, Fox Chase Cancer Center, Philadelphia, Pa.
Semin Oncol; 10(4):366-77 1983

Renal-cell carcinoma usually affects those over 40 years old, and, in any age group, the disease occurs about twice as frequently among men as it does among women. The incidence of the disease has been steadily increasing over the years. In the United States, the probability of surviving after diagnosis of renal cancer has been improving since 1940 regardless of race, sex, and age at diagnosis. The relationship between SES and the chance of developing the disease is sporadic with an indication of a slightly higher risk in the upper socioeconomic classes. Urban/rural comparisons consistently suggest that a higher risk is associated with urban residence. Tobacco use is probably the only environmental factor that could be considered to be etiologically related to cancer of the kidney. A variety of studies point to a moderate but consistent association with tobacco use in the form of cigarette, cigar, or pipe smoking. The excess of the disease in males compared to females and the lower incidence in Mormons may partly be due to the con-

foundings effect of smoking. Dietary vitamin A or vitamin A supplements may have an antipromoting effect in the development of kidney cancer. Hypotheses implicating fat and/or cholesterol intake in the etiology of cancer of the kidney appear to be too tenuous. The evidence of a relationship between concentrations of certain trace metals in drinking water and incidence of renal cancer is weak. Similarly, there is no strong indication of an increased risk among individuals exposed to radiation. In general, with the exception of the observation of an unusually high risk among coke-oven workers, occupational studies have not identified any high-risk groups. Familial aggregation, though rare, occurs with peculiar disease characteristics that may predict similar cancers in the proband's relatives with a high degree of accuracy. In conclusion, the etiology of cancer of the kidney is poorly understood. The descriptive epidemiology of the disease provides some interesting insights into the correlates of the distribution of the disease. (ABSTRACT TRUNCATED AT 400 WORDS) (Author abstract)

91. A POPULATION-BASED CASE-CONTROL STUDY OF RENAL CELL CARCINOMA.

McLaughlin JK, Mandel JS, Blot WJ, Schuman LM, Mehl ES, Fraumeni JF Jr
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JNCI; 72(2):275-84 1984

A population-based case-control study of renal cell carcinoma (495 cases and 697 controls) in the Minneapolis-St. Paul seven-county metropolitan area implicated cigarette smoking as a risk factor with an odds ratio (OR) among men of 1.6 (95% confidence intervals: 1.1-2.4) and among women of 1.9 (1.3-3.0). A statistically significant dose response was observed in both sexes for pack-years of cigarette use. On the basis of calculations of attributable risk, it was estimated that 30% of renal cell cancers among men and 24% among women were due to smoking. High relative adult weight as measured by the body mass index (BMI) was found to be a major risk factor among women but not among men, with those in the highest 5% of the BMI having an OR of 5.9 (1.8-20.4) in comparison to the lowest quartile. This association with excess weight was not seen at age 20, but it became more pronounced with increasing age, suggesting that the primary influence of weight gain is during the late stages of renal carcinogenesis. Excess risks were also related to ethnic background (particularly, German), which may account in part for the elevated incidence of renal cancer in the North Central area of the United States. In addition, positive associations were observed for long-term use of phenacetin-containing analgesics, heavy meat consumption, and heavy tea drinking (females only). An occupational clue was provided by an increased risk for exposure to petroleum, tar, and pitch products. Excesses of certain urologic and cardiovascular diseases were also observed among the cases compared to controls. (Author abstract)

92. INTERNATIONAL TRENDS IN PROSTATIC CANCER.

Zaridze DG, Boyle P, Smans M
Unit of Analytical Epidemiology, International Agency for Research on Cancer, Lyon, France.
Int J Cancer; 33(2):223-30 1984

The most recent data available demonstrate a 120-fold difference between the lowest and highest incidence rates of prostatic cancer, the disease being very common in North America, particularly among Blacks, and in Scandinavia, while it is rare in Japan and other oriental countries. The highest mortality for prostatic cancer is reported from St. Vincent and Grenadines, Martinique and Bermuda, from countries where the morbidity

statistics are not available; the mortality rates reported from the United States and Canada are considerably lower. The incidence of and mortality from prostatic cancer have increased in most countries, in particular in areas with an initially low frequency of this disease. The ratio of mortality to incidence for prostatic cancer varies rather widely, being low in North America, Hawaii and Scandinavia. It is suggested that the observed variation in the mortality to incidence ratio for prostatic cancer could be due to differences in diagnostic practices between countries. This could explain, at least in part, the fact that the increasing trends of prostatic cancer incidence in North America are not accompanied by an increase in mortality from this tumour. This notion, however, does not exclude advances in treatment as possible determinants of the improved survival rate from prostatic cancer in this part of the world. The available statistics on prostatic cancer are based on the sum of clinically diagnosed carcinomas and those latent tumours found unexpectedly at prostatectomy and autopsy. The proportion of latent carcinomas among all prostatic cancer cases depends on the detection rate and varies from country to country, thus casting uncertainty on the comparability of prostatic cancer statistics from different areas. To avoid confusion in the statistics of prostatic cancer, it would be useful to consider introducing latent prostatic cancer as a separate entity in the next revision of the International Classification of Diseases (ICD). (Author abstract)

93. OVARIAN CANCER. GEOGRAPHICAL, HOST AND ENVIRONMENTAL FACTORS. AN OVERVIEW.

Anteby SO, Mor Yosef S, Schenker JG
Department of Obstetrics and Gynecology, Hadassah University Medical Center, Ein Karem, Jerusalem, Israel.
Arch Gynecol; 234(2):137-48 1983

The incidence of ovarian cancer is reviewed among different races and ethnic groups. We present the effect of socio-economic class, age, endocrinological factors, menstrual cycle, reproductive history, familial, and genetic factors, viral infections, chemical carcinogens, and previous exposure to radiation on the incidence of ovarian cancer. There is evidence that environmental factor affects the distribution of various types of ovarian cancer. Migration may also change the susceptibility to this disease and the mean age was varied between countries being lowest where incidence was highest. The disease appeared to have a familial incidence. The protective effect of oral contraceptive steroids and the role of asbestos as a chemical carcinogen are discussed. (Author abstract) (86 Refs)

94. PREDILECTION OF LUNG CANCER FOR THE UPPER LOBES: AN EPIDEMIOLOGIC INQUIRY.

Byers TE, Vena JE, Rzepka TF
Department of Social and Preventive Medicine, School of Medicine, State University of New York at Buffalo.
JNCI; 72(6):1271-5 1984

Data from 24,798 cases of primary neoplasm of the lung registered by the Surveillance, Epidemiology, and End Results Program between 1973 and 1977 were examined for the demographic determinants of lobe of origin. Lung cancer occurred predominantly in the upper lobes in both sexes, in both blacks and whites, and at all ages. This pattern was observed for squamous cell and small cell carcinoma as well as adenocarcinoma. The predominance of lung cancer in the upper lobes was much stronger in the young and somewhat stronger in blacks. These findings are discussed in light of current theories of pulmonary carcinogenesis. Current theories may not explain entirely these