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1 AU - Clemens MR ; Frank H ; Rammer H ; Waller HD
AD - Medizinische Klinik, Abt. II, Institut fur Toxikologie der Universitat 2, Tubingen, W. Germany
TI - VINYLCHLORIDE: A CARCINOGENIC METABOLITE OF BCNU (MEETING ABSTRACT).
SI - HERN/83/00917
SO - Blut; 45:233 1982
LA - ENG
AB - The production of vinyl chloride was first observed during experiments on the metabolism of BCNU (Carmustine). Erythrocytes were incubated with BCNU (75 uM) in head space vials. Gases in the head space were analyzed by gas chromatography and mass spectrometry. Vinyl chloride and acetylene were identified. Vinyl chloride develops from 1,3-bis (2 chloroethyl)-1-nitrosourea in red blood cells by cleavage of 2 chloroethyl groups of nitrosourea. This reaction is not influenced by superoxide anions since addition of superoxide dismutase (50-500 Units) did not alter the development of vinylchloride. The production of vinyl chloride from BCNU is important because it is known to be a strong carcinogen. (no Refs)

2 AU - Versen P
AD - Employment Accident Insurance Fund of the Chemical Industry, Gaisbergstrasse 7, D 6900 Heidelberg, W. Germany
TI - VINYL CHLORIDE DISEASE IN THE FEDERAL REPUBLIC OF GERMANY DEVELOPMENT - COUNTER-MEASURES - PRESENT SITUATION - CONCLUSION (MEETING ABSTRACT)
SI - HERN/82/19119
SO - Eighth International Conference of Occupational Health in the Chemical Industry, Sept 22-25, 1980, Tokyo Permanent Commission and International Association on Occupational Health, pp. 55-06, 1980.
LA - ENG
AB - Only since 1972 have cases of people being taken ill due to exposure to vinyl chloride (VC) been registered in the Federal Republic of Germany. The number of reported cases reached a peak of 121 in 1974; in 1979 there were only 4 cases. Altogether 319 cases were to be judged. In 102 cases an occupational disease was recognized. Of these, 38 cases were slight, 26 moderately severe, 23 severe and 15 died of a hemangiosarcoma of the liver. A survey of the counter-measures introduced is given, eg with regard to reduction of exposure and occupational medical check-ups. The results are classified. Fibrosis of the lungs due to polyvinyl chloride (PVC) dust could not be found. It is still under discussion whether cases of encephalopathy are to be recognized as a result of VC intoxication. So far no satisfactory explanation could be found why the people taken ill are distributed so unevenly over the individual factories which produce PVC. Yet even if certain things remain unexplained, it seems justified nowadays in respect of vinyl chloride disease to say "Recognizing a risk is a major step towards eliminating it". (no Refs)

3 AU - Thiess AM ; Link R
AD - BASF Aktiengesellschaft, Occupational Medicine and Health Protection, 6700 Ludwigshafen, Rhine, Federal Republic of Germany
TI - EPIDEMIOLOGICAL MORTALITY STUDIES IN THE CHEMICAL INDUSTRY BASF AKTIENGESELLSCHAFT, LUDWIGSHAFEN, FEDERAL REPUBLIC OF GERMANY (MEETING ABSTRACT)
SI - HERN/82/15058
SO - Eighth International Conference of Occupational Health in the Chemical Industry, Sept 22-25, 1980, Tokyo Permanent Commission and International Association on Occupational Health, pp. S4-09, 1980.
LA - ENG
AB - Epidemiological mortality studies have been undertaken in the BASF since 1974. The program covers prospective mortality studies on skilled chemical workers, emanating from exposure to health-impairing substances. A significant increase in the number of observed cases of cancer deaths in comparison to the expected cancer rate was only found in the trichlorphenol-dioxin cohort which was exposed to dioxin after an accident in 1953. A clear but not significant increase of observed against expected cancer deaths was found in the truck driver cohort. Only a slight increase in the number of cancer deaths could be observed in the cohorts with exposure to auramine, ortho-phthalodinitrile, vinyl chloride and vinylidene chloride. No increased rates of cancer deaths were found in the cohorts exposed to cadmium, chloroquinone, di-2-ethylhexylphthalate, ethylbenzene residue and styrene. Due to the high rate of mixed exposures it is difficult to evaluate the results in the case of acrylonitrile which is suspected to be a carcinogenic risk to man. (no Refs)

4 AU - Nakayama E ; Nishizawa T ; Shibata T ; Nagano K ; Oobayashi H
AD - Occupational Health Service Center, 35-1, 5-chome, Shiba Minato-ku, Tokyo, Japan
TI - CHRONIC INHALATION TOXICITY OF VINYL CHLORIDE MONOMER (MEETING ABSTRACT)
SI - HERN/82/15054
SO - Eighth International Conference of Occupational Health in the Chemical Industry, Sept 22-25, 1980, Tokyo Permanent Commission and International Association on Occupational Health, pp. S2-01, 1980.
LA - ENG
AB - Two groups of Wistar rats, each consisting of 32 males and 32 females, were exposed to air containing 0 (control) and 3000 ppm vinyl chloride monomer (VCM), 4 hr/day, 5 days/week for a period of 52 weeks. After 13 and 26 weeks each time 8 male and 8 female rats per group and after 52 weeks all alive animals were killed for detailed examinations on growth, mortality, hematology, clinical chemistry, organ weights and pathomorphology of various organs. By 26 weeks of exposure no significant changes were disclosed between the control and test animals. In the latter half of the experiment mortality of exposed rats rose gradually and of 32 tested rats 15 survived 52 weeks with tumors in 14

rats, while in the control group all were alive with no malignant neoplasm. Primary neoplasms explaining causes of death were noticed in such various sites as the lungs, liver, nasal cavity, ceruminous and mammary glands and so on. Besides in the kidneys histological changes were found. Growth of exposed rats retarded slightly. Hematological and biochemical blood changes, however, were very slight even after 52 weeks except minor signs of anemia. In this study obvious parameters for early diagnosis of VCM related changes could not be found, partly because our examinations aimed at detecting hepatic changes, that were revealed in only 4 rats. (no Refs)

5 AU - Fleig I ; Thiess AM
AD - BASF Aktiengesellschaft, Occupational Medicine and Health Protection, 6700 Ludwigshafen, Rhine, W. Germany
TI - CHROMOSOME ANALYSES IN THE CHEMICAL INDUSTRY - PREVENTIVE METHODS IN OCCUPATIONAL MEDICINE (MEETING ABSTRACT)
SI - NERN/82/15053
SO - Eighth International Conference of Occupational Health in the Chemical Industry, Sept 22-25, 1980, Tokyo Permanent Commission and International Association on Occupational Health, pp. 5-10, 1980.
LA - ENG
AB - In 1970 chromosome analyses were started in the BASF Aktiengesellschaft on workers who could come into contact with lead or other toxic substances, such as ethylenelmine, benzene, dimethylsulphate. These investigations were undertaken in order to determine whether or not chemical substances which possibly show a mutagenic effect in bacterial tests or animal experiments, can also cause mutations in human beings. The chromosome analyses were performed on lymphocytes which were cultured for 72 hours and then handled according to a modification of the Moorhead et al method. At least 100 metaphases per person were analysed. The following substances were examined: acrylonitrile, auramine, benzene, ethylenelmine, alkylene oxides (ethylene oxide, propylene oxide and derivatives), ethylbenzene residue, di-2-ethylhexylphthalate, dimethylsulphate, lead, dimethylcarbamoylchloride, ortho-phthalodinitrile, styrene, dioxane, tetrahydrofurane, tetrachlordibenzodioxin, vinyl chloride. Increased rates of chromosome aberrations were found in 1 case of angiosarcoma and 20 other workers from various German chemical plants (not BASF) due to vinyl chloride (VC)-exposure, in persons employed in plants processing unsaturated polyester resins (also not BASF) and in workers with longterm exposure to alkylene oxides. The remaining cytogenetic studies showed no increased aberration rates. (no Refs)

6 AU - National Toxicology Program
AD - Box 12233, Research Triangle Park, NC, 27709
TI - CARCINOGENESIS BIOASSAY OF BUTYL BENZYL PHTHALATE (CAS NO. 85-68-7) IN F344/N RATS AND B6C3F1 MICE (FEED STUDY).
SI - ICDB/82/32309
SO - Natl Toxicol Program Tech Rep Ser. Issue 213, 98 pp., 1982.
LA - ENG
AB - A carcinogenesis bioassay of butyl benzyl phthalate, (BBP) a plasticizer for vinyl chloride plastics was conducted by feeding diets containing 6,000 or 12,000 ppm BBP to 50 F344/N rats and 50 B6C3F1 mice of each sex for 28-103 wk. Mean body weights of dosed female rats and mice of both sexes were lower than those of controls throughout most of the study. After wk 14, an increasing number of dosed male rats died of internal hemorrhaging, and all survivors were killed at wk 29-30. BBP could not be adequately tested for carcinogenicity in male F344/N rats. Mononuclear cell leukemias occurred at a statistically significant increased incidence in the high-dose group of female rats when compared with the control group, and with a significantly increasing trend. These results remained significant when compared with the historical incidence for F344/N female rats with leukemia. The leukoproliferation was generally characterized by splenomegaly and often by hepatomegaly. Administration of BBP was not associated with increased incidences of any type of tumor among male and female mice. Tumor rates were decreased in female rats for fibroadenomas of the mammary glands and in male mice for lymphomas of the hematopoietic system and for alveolar/bronchiolar adenomas or carcinomas. Under the conditions of this bioassay, BBP was probably carcinogenic for female F344/N rats, causing an increased incidence of mononuclear cell leukemias. The male F344/N rat study was considered inadequate for evaluation due to compound-related toxicity and early mortality. BBP was not carcinogenic for B6C3F1 mice of either sex. (47 Refs)

7 AU - Green M
AD - Chemical Procurment for Res., Polaroid Corporation, Cambridge, MA, 02139
TI - SCIENTIFIC MCCARTHYISM.
SI - ICDB/82/30751
SO - Chemtech; 11(17):402-406 1981
LA - ENG
AB - Loss of objectivity in the filed of cancer research is discussed. Topics include the increased public awareness of environmental chemicals, government regulation without review of interpretation of experimental results, high- rather than low-level experimental exposure and the need to establish threshold doses, danger of extrapolation to low doses when curve shape is not known, use of cancer-prone test animals as models for human exposure, and the tendency to regard positive (even false-positive) results more highly than negative findings. The chemicals sodium nitrite, thiouracil, 6-nitro-benzimidazole, and vinyl chloride are used to

illustrate certain points. Stress as a cause for increased cancer incidence is noted. Prediction of cancer in humans must be followed by validation of actual experience: dose-response at realistic levels of exposure, threshold level, and processes by which cancer develops need to be elucidated. (9 Refs)

8 AU - Juszczyk J
AD - Klinika Chorob Zakaznych, Akademia Medyczna, ul. Wincentego 1, 61-003 Poznan, Poland
TI - ECOLOGIC PROBLEMS IN HEPATHOLOGY. CHRONIC LIVER DAMAGE DUE TO ENVIRONMENTAL FACTORS.
SI - ICDB/82/30742
SO - Pol Arch Med Wewn; 67(3):101-112 1982
LA - POL
AB - Studies on the harmful effects of environmental factors on the liver are reviewed after an outline of the biotransformation processes taking place in the liver. Substances with proven or suspected hepatocarcinogenic effects include mycotoxins, such as aflatoxins, safrole, vinyl chloride, and active agents of oral contraceptives. Increased frequency of hepatic carcinoma was found in rats treated with 0.000075% aqueous solution of a nitrosamine po compared with untreated controls. Liver scirrhoma, induced by many environmental agents, is a substrate for the development of hepatic carcinoma. (38 Refs)

9 AU - Hall JA ; Saffhill R
AD - Christie Hospital and Holt Radium Institute, Manchester, England
TI - CHLOROACETALDEHYDE, A VINYL CHLORIDE METABOLITE, INDUCES ERRORS DURING IN VITRO DNA SYNTHESIS (MEETING ABSTRACT)
SI - HERN/82/12891
SO - Br J Cancer; 44(2):272 1981
LA - ENG
AB - Chloroacetaldehyde (CA), a rearranged metabolic product of the human carcinogen vinyl chloride, has been shown to be mutagenic in certain microbial systems as well as towards mammalian cells. CA has been reacted with the alternating DNA-like polymers poly(dA-dT) and poly(dC-dG) when, as with DNA, ethano-adducts of the adenine and cytosine bases are formed. These treated polymers, when used as templates for Escherichia coli DNA polymerase I, show a decreased ability to direct DNA synthesis. This is accompanied by an increase in the relative levels of non-complementary nucleotides incorporated into the newly synthesized DNA-like material. This increased with the amount of modified base present in the templates used. With the poly(dA-dT) templates one dGMP (guanosine monophosphate) residue was incorporated for every 60 +/- ethenoadenine residues present, while no dCMP (cytidine monophosphate) misincorporation was detected. One misincorporation of dAMP or dTMP (thymidine monophosphate) occurred in the presence of 30 +/- and 80 +/- ethenocytosine residues respectively in the poly(dC-dG) templates. For the modified poly(dC-dG) templates, a nearest-neighbor analysis shows that the majority of the errors were incorporated opposite the cytosine (or modified cytosine)

bases. Extensive analyses of the modifications present in the templates indicate that the misincorporations observed are not due to the presence of apurinic sites or to the formation of uracil or xanthine by deamination of the cytosine or adenine bases respectively. We conclude that the non-complementary nucleotide incorporations probably arise from the presence of etheno-adducts in the templates used. (no Refs)

10 AU - Latarjet R
AD - Institut Curie, Paris, France
TI - QUANTITATIVE COMPARISON OF GENOTOXIC (MUTAGENIC AND CARCINOGENIC) RISKS AND THE CHOICE OF ENERGY SOURCES.
SI - ICDB/82/29002
SO - Bull Acad Natl Med (Paris); 166(2):181-201 1982
LA - FRE
AB - The mutagenic and carcinogenic effects of pollution are discussed in relation to energy forms. The need for determination and comparison of risks for various energy forms is considered. Risks should be considered as both relative and absolute and in relation to both self and others. Genotoxic risks include lethal, mutagenic, and carcinogenic effects. When considering the carcinogenic effects baseline statistics must be considered. In industrialized countries, 20% of population will eventually die of cancer; another 6% will be cured of cancer. The system of rad-equivalences is considered in relation to the mutagenic effects of vinyl chloride, formaldehyde, ethylene, and ethylene oxide. Using the rad-equivalence concepts it is possible to extrapolate the rules developed for ionized radiation to determine persons at high risk for mutagenic effects of various chemicals. The system is particularly relevant for persons exposed to ethylene and ethylene oxide. The levels of pollution due to ethylene and ethylene oxide in France are described. It is recommended that controls be established for the main genotoxic chemical pollutants and that long term risks be assessed in relation to nuclear energy and energies obtained by combustion. (2 Refs)

11 AU - Wallace D ; Nelson N ; Gates T
AD - Public Interest Scientific Consulting Service, 549 W. 123 St., New York, NY, 10027
TI - POLYVINYL CHLORIDE WIRE INSULATION DECOMPOSITION II. CONSIDERATION OF LONG TERM HEALTH EFFECTS FROM CHLORINATED HYDROCARBONS.
SI - ICDB/82/29292
SO - J Combust Toxicol; 9(May):105-112 1982
LA - ENG
AB - Because of continued reports of new disorders in female survivors of the Beverly Hills Supper Club Fire and in the firefighters injured during the New York Telephone Fire and who were on active duty 1970-June 1931, further studies of the possible long-term health effects were conducted. All 12 women among the 50 injured survivors of the Beverly Hills Fire, who were of reproductive age (40 yr or less), responded to a letter of inquiry. All complained

of uterine dysfunctions: eight complained of heavy menstrual bleeding and three had hysterectomies. Two miscarriages occurred but no other pregnancies or births. The 12 reported no such pre-fire problems. A total of six cancer cases were uncovered among the 700 firefighters involved in the New York fire. Cancer occurred in 4/6 cases in men less than 45 yr old compared to 35/62 in the fire department as a whole for men greater than 45 yr old. Three of four cases of laryngeal/throat lesions reported for the department were in the exposed group. While the overall cancer incidence is only slightly higher for the cohort (857/100,000) than for the department (560/100,000), the age specific incidences are much higher if the assumption of similar age structure of the two populations is valid. The literature on the health effects of vinyl chloride monomer and chlorinated aromatic hydrocarbons includes reports on uterine dysfunction and occurrence of rare cancer types. The possibility that the presence of these compounds in the smoke may be producing or promoting the observed patterns is addressed. (16 Refs)

12 AU - Jones DB ; Smith PM
AD - Dept. Gastroenterology, Llandough Hosp., Penarth, S. Glamorgan, England
TI - PROGRESSION OF VINYL CHLORIDE INDUCED HEPATIC FIBROSIS TO ANGIOSARCOMA OF THE LIVER.
SI - ICDB/82/28032
SO - Br J Ind Med; 39(3):306-307 1982
LA - ENG
AB - Two vinyl chloride monomer (VCM) workers, who developed non-cirrhotic portal fibrosis and portal hypertension, died from angiosarcoma of the liver 5 and 10 years later respectively, despite withdrawal from occupational exposure. We suggest that non-cirrhotic portal fibrosis caused by exposure to VCM is potentially premalignant and that those workers who already have the condition should be carefully monitored. (Author abstract) (11 Refs)

13 AU - Anderson D
AD - BIBRA, Woodmansterne Road, Carshalton, England
TI - THE PREDICTABILITY OF ANIMAL BIOASSAYS (MEETING ABSTRACT).
SI - HEPN/82/19979
SO - Twelfth Annual Meeting of the European Environmental Mutagen Society, June 20-24, 1982, Otpoli, Espoo, Finland. European Environmental Mutagen Society 250 pp., 1982.
LA - ENG
AB - Laboratory models which provide data for predicting the potential human mutagenic or carcinogenic risk of chemicals are short-term tests, animal studies or cellular responses combined with human exposures. The efficiency of the models can be judged by their ability to predict a human mutagen or carcinogen, its potency and organ specificity. Cigarette smoke, vinyl chloride, lead and anesthetic gases have the best documented evidence of possible mutagenic effects in man. There are 26 agents which are known to produce cancer in man but only 19 of these are specific chemicals

which are also known to be animal carcinogens. Laboratory models are generally judged on interspecies comparisons involving species other than man. Short-term tests can have as high as 90% predictivity for animal carcinogenicity but this is influenced by chemical selection and test conditions. Comparisons in rats and mice of carcinogenicity data show these species to be 85% predictive for each other. About 60% of human carcinogens have the same target organ in man and animal studies. Sixty-five percent of chemicals carcinogens in rats and mice have a common target organ in both species. Short-term tests are not sufficiently developed to predict organ specificity. Potency correlations from short-term tests to animal models are subject to inaccuracies partly because of the variables associated with methods expressing dose and response in animal studies. (no Refs)

14 AU - Dent JG ; Graichen ME
AD - Smith Kline and French Laboratories, P.O. Box 7929, Philadelphia, PA, 19101
TI - EFFECT OF HEPATOCARCINOGENS ON EPOXIDE HYDROLASE AND OTHER XENOBIOTIC METABOLIZING ENZYMES.
SI - ICDB/82/27564
SO - Carcinogenesis; 3(7):733-730 1982
LA - ENG
AB - Hepatocarcinogens cause marked biochemical changes in the liver at short intervals after administration. The studies described were designed to investigate the effects of hepatocarcinogens and hepatotoxicants on the microsomal mixed function oxidase system, DT-diaphorase and epoxide hydrolase. Following 5 day po treatment of male F-344 rats with aflatoxin B1 (AFB), 2-acetylaminofluorene (AAF), technical grade dinitrotoluene (DNT), or 2,4-diaminotoluene, microsomal cytochrome P450 dependent enzyme activities were depressed while epoxide hydrolase activity was markedly elevated (3-8 times control). Diethylnitrosamine (DEN) given at 5 mg/kg/day and DL-ethionine at 1,000 mg/kg/day failed to increase epoxide hydrolase. 3-Methylcholanthrene, methylnitrosourea, carbon tetrachloride, bromobenzene and vinyl chloride all failed to increase epoxide hydrolase activity. Using 3 daily ip injections, dose-response relationships for increases in epoxide hydrolase were generated for the hepatocarcinogens. With the exception of p-dimethylaminoazobenzene (DAB) and DEN, the carcinogens studied produced log-linear dose response curves for increase in epoxide hydrolase. Both DEN and DAB caused increased in epoxide hydrolase but classical sigmoidal dose-response curves were not obtained. The order of potency for increasing epoxide hydrolase was AFB much greater than AAF greater than 2,6-dinitrotoluene greater than 3'-methyl-N,N-dimethyl-4-aminoazobenzene greater than DNT greater than 2,4-dinitrotoluene. The slopes of the linear portions of the log dose-response curves were not statistically different from the slope of the dose-response curve obtained with AAF suggesting that structurally diverse carcinogens elicit increases in epoxide hydrolase by a common mechanism. (Author abstract) (46 Refs)

15 AU - Oesch F ; Doerjer G
AD - Dept. Toxicology, Univ. Mainz, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany
TI - DETECTION OF N2,3-ETHENOGUANINE IN DNA AFTER TREATMENT WITH CHLOROACETALDEHYDE IN VITRO.
SI - ICDB/82/26749
SO - Carcinogenesis; 3(6):663-665 1982
LA - ENG
AB - The reaction of chloroacetaldehyde, a reactive metabolite of the carcinogen vinyl chloride, with DNA produces in addition to the hitherto known adducts, 1,N6-ethenoadenine and 3,N4-ethenocytosine, an ethenoguanine adduct, namely N2,3-ethenoguanine. This adduct is formed in the reaction of chloroacetaldehyde with the free base as well. After DNA hydrolysis followed by isolation of this new adduct by hplc, its mass spectrum and fluorescence spectrum are identical with those published in the literature for the chemically synthesized N2,3-ethenoguanine. The formation of only this guanine derivative out of several theoretically possible reaction products allows the formulation of a reaction scheme. The absence of 7-(2-oxoethyl)-guanine, another recently detected DNA adduct of viny chloride, in chloroacetaldehyde-treated DNA suggests its origin from the other reactive metabolite of vinyl chloride, chloroethylene oxide. The potential of N2,3-ethenoguanine to lead to misincorporation of deoxythymidine monophosphate opposite to guanine and the high fluorescence of this adduct provide it with potentially high biological significance and ease of analytical monitoring. (Author abstract) (14 Refs)

16 AU - Maltoni C ; Ciliberti A ; Carretti D
AD - Inst. Oncology, Bologna, Italy
TI - EXPERIMENTAL CONTRIBUTIONS IN IDENTIFYING BRAIN POTENTIAL CARCINOGENS IN THE PETROCHEMICAL INDUSTRY.
SI - ICDB/82/26015
SO - Ann NY Acad Sci; 381:216-249 1982
LA - ENG
AB - Incidence of brain tumors was studied in Sprague-Dawley rats treated by inhalation at different doses of vinyl chloride (VC), vinylidene chloride (VDC), ethylene dichloride, acrylonitrile (AC), styrene (ST), propylene, trichlorofluoromethane, dichlordifluoromethane, and chlorodifluoromethane. VC was also studied in some Wistar rats and for different times and schedules. Some compounds in olive oil were studied by gavage: VC, VDC, AC, ST, styrene oxide, vinylidene fluoride, trichloroethylene, benzene, asbestos (crocidolite), and polyvinyl chloride. VC and AC caused neuroblastomas and gliomas (oligodendrogliomas), respectively, when given by inhalation. Such effects were not seen at concentrations of VC of 500 ppm or below and with AC at 10 ppm and below. This concentration-related effect on tumor incidence appears less evident when total incidence is considered without regard to dose and type of tumor. Under the conditions of the experiments, none of the compounds

given by gavage produced brain tumors. (11 Refs)

17 AU - Wen CP ; Tsai SP ; Gibson RL
AD - Gulf Science and Technology Co., P.O. Box 2100, Houston, TX, 77001
TI - A REPORT ON BRAIN TUMORS FROM A RETROSPECTIVE COHORT STUDY OF REFINERY WORKERS.
SI - ICDB/82/26007
SO - Ann NY Acad Sci; 381:130-133 1982
LA - ENG
AB - Standardized mortality ratio (SMR) analysis was conducted for a total of 17,521 employees of one full-service refinery in Texas, at which fuels, lubricants, and various petrochemicals, but not vinyl chloride, were manufactured. Vital status was successfully determined for nearly 90% of the male employees; 4,766 deaths were recorded for the study period (1935-79). The overall SMR for the population was 0.89 for all causes of death, and 0.97 for malignant and benign brain neoplasms. There were 30 brain tumor deaths, malignant, benign, or of unspecified nature; 25 in white males and 5 in nonwhite males; the worker population was 17% nonwhite. Age at death for the 30 brain tumor patients averaged 57.2 yr; the mean year of hire was 1934; and the mean year of death was 1966. Length of employment for the group with brain tumors ranged from 8 days to 43 yr, with a mean of 23 yr. A preliminary survey of job assignments of those workers dying from brain tumor has not revealed any significant clustering compared to the total cohort. A separate study of 443 benzene workers employed from 1952-76, 1,005 solvent-dewaxing workers employed from 1935-76, and a control group of 2,140 workers at the same plant, revealed no significant excess brain cancer in any group. There seems to be no significant increased risk of brain tumor among workers at this Texas refinery. (18 Refs)

18 AU - Alexander V ; Laffingwell SS ; Lloyd JW ; Waxweiler RJ ; Miller RL
AD - Occupational Safety and Health Admin., United States Dept. Labor, Washington, DC, 20210
TI - INVESTIGATION OF AN APPARENT INCREASED PREVALENCE OF BRAIN TUMORS IN A U. S. PETROCHEMICAL PLANT.
SI - ICDB/82/25866
SO - Ann NY Acad Sci; 381:97-107 1982
LA - ENG
AB - The occurrence of 20 primary brain cancer deaths among workers in a moderate-sized petrochemical production facility in Texas prompted a cohort mortality study and a brain tumor case-control study. The av age at death was 55 yr and the total length of employment ranged from 1 mo to greater than 35 yr, with a median value of 19 yr. The interval from first employment to death ranged from 3.5 yr to almost 36 yr, with a median of 24 yr. All cases were males; 18 were white, 2 black. All but one were native-born Americans. Comparison with county primary brain tumor death statistics revealed an approx plant-wide risk about 2x that of the county as a whole. Sixteen of the cases were identified as glioblastoma multiforme. No common job title, department code, or chemical exposure could be found in careful preliminary

examination of the work histories of the affected employees. Potential suspect agents which could be responsible for the unusual occurrence of brain cancer at this plant include vinyl chloride and diethyl sulfate; however, careful examination of the work histories did not support a significant positive association with vinyl chloride. These tumors are likely the result of occupational chemical exposures since there is no good evidence implicating nonplant, general environmental factors as the cause of brain cancer excess. (57 Refs)

19 AU - Shibuya H ; Horiuchi J ; Suzuki S ; Takeda M
AD - Dept. Radiology, Tokyo Medical and Dental Univ. Sch. Medicine, Tokyo, Japan
TI - REAPPRAISAL OF RADIOTHERAPY FOR LARYNGEAL CANCER USING TREATMENT CAST.
SI - ICDB/82/25468
SO - Nippon Igaku Hoshasen Gakkai Zasshi; 42(2):200-202 1982
LA - JPN
AB - The use of vinyl chloride shells to improve the accuracy of radiotherapy for laryngeal carcinoma is discussed with respect to 12 patients who were treated using the shells and 21 who were treated using a free set up. An apparatus to automatically make the shells using a vacuum-forming technique was introduced. No large differences in dose received were observed between the two groups. Edema was a complication in 3/12 shell patients and no complications were observed in the 22 free set up patients. On the other hand, no recurrence was observed 6-29 mo after treatment in the shell group while recurrance was observed 8-62 mo after treatment in the free set up patients. (9 Refs)

20 AU - Laib RJ ; Bolt HM
AD - International Agency for Research on Cancer, 69372 Lyon Cedex 2, France
TI - INDUCTION OF HEPATOCELLULAR NUCLEOSIDE-5'-TRIPHOSPHATASE (ATPASE) DEFICIENT FOCI BY VINYL CHLORIDE (VC) (MEETING ABSTRACT).
SI - HERN/82/17216
SO - Proc Am Assoc Cancer Res; 23:231 1982
LA - ENG
AB - In many species including man, VC induces angiosarcomas originating from endothelial cells of the liver, while in newborn rats, hepatocytes are more susceptible. This effect can be quantified by evaluating preneoplastic hepatocellular foci with ATPase deficiency. Rats were exposed to 2000ppm VC (8hrs/day), either transplacentally (schedule A) or immediately after birth for different time intervals (B-E), and from the age of 21 days onwards (F). Four-month old animals were sacrificed and the livers evaluated histochemically for ATPase deficient foci. Transplacental exposure (A) and schedule B revealed no increase in ATPase deficient foci, possibly due to the low rate of VC metabolism at this developmental stage. The % foci increased from schedule C to D but was not further enhanced after prolonged exposure (E). Only a few ATPase deficient foci were observed when exposure started 21 days after birth (F). As shown previously, a

70 day exposure of adult female rats to VC also did not result in ATPase deficient foci. These results indicate that the initiation of preneoplastic lesions of VC in rat hepatocytes is restricted to the early lifetime and that VC does not exert a substantial growth-promoting effect on induced ATPase deficient foci. (1 Ref)

21 AU - Air Pollution Control Association
AD - Pittsburgh, PA
TI - PROCEEDINGS OF THE INTERNATIONAL TECHNICAL CONFERENCE ON TOXIC AIR CONTAMINANTS: HEALTH EFFECTS MONITORING AND CONTROL HELD IN NIAGARA FALLS, NY, 9-10 OCTOBER, 1980.
SI - ICOB/82/23628
SO - Proceedings of the International Technical Conference on Toxic Air Contaminants: Health Effects Monitoring and Control held in Niagara Falls, NY, 9-10 October, 1980. Pittsburgh, Air Pollution Control Association, 247 pp., 1980.
LA - ENG
AB - Monitoring and control of toxic air contaminants were discussed in the following presentations: air pollution evaluation using risk assessment technology, potential model of carcinogenesis and interpretation of short term tests, a working model of carcinogenesis and interpretation, Environmental Protection Agency (EPA) carcinogen policy, developing neighborhood air concentration standards, measurement of perchloroethylene in ambient air, ambient air measurements of benzene in the bistate New York-New Jersey region, toxic and carcinogenic air pollutants in New Jersey (volatile organic substances), polynuclear aromatic hydrocarbon losses during high vol sampling, monitoring a chlorine spill, regulation of the incineration of hazardous wastes, control of vinyl chloride emissions in the Goodyear Niagara Falls polyvinyl chloride plant, problems and pitfalls of disposal of hazardous wastes, control technics for gas emissions from hazardous waste landfills, EPA regulation of atmospheric carcinogens, and regulatory framework for setting air emission limits for non-criteria pollutants. (51 Refs)

22 AU - Ribovich ML ; Miller JA ; Miller EC ; Timmins LG
AD - (c/o Miller) McArdle Lab. Cancer Res., Univ. Wisconsin Center Health Sciences, 450 North Randall Ave., Madison, WI, 53706
TI - LABELED 1,N(6)-ETHENOADENOSINE AND 3,N(4)-ETHENOCYTIDINE IN HEPATIC RNA OF MICE GIVEN [ETHYL-1,2-3H OR ETHYL-1-14C] ETHYL CARBAMATE (URETHAN).
SI - ICOB/82/22605
SO - Carcinogenesis; 3(5):539-546 1982
LA - ENG
AB - Injection of a single dose of [ethyl-1,2-3H] or [ethyl-1-14C]ethyl carbamate into 12-day old male (C57BL/6 x C3H/He)F1 mice or of [ethyl-1,2-3H]ethyl carbamate into adult male A/Jax mice resulted in the formation of labeled 1,N6-ethenoadenosine and 3,N4-ethenocytidine adducts in the hepatic RNA. These adducts were characterized by comigration on hplc of 3H or 14C in enzymatic hydrolysates of the RNA with synthetic standards. Both the ethenoadenosine and ethenocytidine

were further characterized by their conversion to acetylated products that comigrated with acetylated synthetic standards. The ethenoadenosine was also converted by anhydrous trifluoroacetic acid to a product that comigrated with synthetic 1,N6-ethenoadenine. The levels of adducts in the hepatic RNA 12 hr after a single injection of 0.5-0.6 mg of ethyl carbamate/g body wt were 6-10 and 2-3 pmol/mg RNA of ethenoadenosine or ethenocytidine, respectively. No labeled ethenoadenosine or ethenocytidine could be detected in the hepatic RNA of mice given [1-14C]ethanol, an enzymatic hydrolysis product of ethyl carbamate. These data indicate that ethyl carbamate may be metabolically activated by dehydrogenation to vinyl carbamate and subsequent epoxidation of the latter compound as previously proposed. Vinyl carbamate epoxide may form etheno derivatives in a manner analogous to that demonstrated for chloroethylene oxide, an electrophilic metabolite of vinyl chloride. Vinyl carbamate has been shown to have the same spectrum of tumor induction as ethyl carbamate but to be much more active than the latter carcinogen. (Author abstract) (37 Refs)

23 AU - Jensen HM ; Chen I ; DeVault M ; Lewis AE
AD - Department of Pathology, School of Medicine, University of California, Davis, CA
TI - ANGIOGENIC BREAST TISSUE AND SECRETIONS IN WOMEN (MEETING ABSTRACT)
SI - HERN/82/13982
SO - 71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.
LA - ENG
AB - Ability to evoke new vessel formation is a property of malignant tissue. Angiogenic factor is a proposed marker for cancerous transformation. Histologically normal lobules and atypical lobules (papillomatosis) were identified and isolated from fresh, sterile tissue stained with 2 mg per 100 ml of methylene blue chloride for 90 minutes at 4 C. Fragments, transplanted onto rabbit irises, were observed for development of delicate vessels around them. On day 5 they were processed for light microscopy. From 34 cancer-associated breasts, 42 of 150 normal lobules (28 per cent) and 22 of 37 atypical loubles (60 per cent) were angiogenic. From 45 women with noncancerous breasts, 39 of 292 normal lobules (13 per cent) and seven of 21 atypical lobules (29 per cent) were angiogenic. Thus, angiogenic parenchyma is more abundant in breast cancer patients. Breast cyst fluids were incorporated in ethylene-vinyl acetate copolymer (Elvax 40, Dupont) and implanted in rabbit corneas. Angiogenesis, occurring in 12 of 21 samples, indicates secretion of angiogenic factor. (no Refs)

24 AU - Popper H ; Maltoni C ; Selikoff IJ
AD - Stratton Lab. for the Study of Liver Disease, Mount Sinai Sch. Medicine, City Univ. New York, New York, NY
TI - VINYL CHLORIDE-INDUCED HEPATIC LESIONS IN MAN AND RODENTS. A COMPARISON.
SI - ICDB/82/21460
SO - Liver; 1(1):7-20 1981
LA - ENG
AB - Parallel sequences in the liver of man, rats, and mice exposed to vinyl chloride (VC) were compared to review pathologic features induced, to document similarities in evolution from precursor lesions to malignant states, and to compare the evolution with that caused by other carcinogenic agents. Available for study were 19 human cases of angiosarcoma and precursor lesions following exposure to VC, previously reported, plus 5 additional angiosarcomas (autopsy) and 16 precursor lesions (biopsy material). Rats and mice had been exposed to VC in inhalation chambers. In man, the number of sinusoidal cells conspicuously increased and they almost filled the spaces between the enlarged hepatocytes. In rodents, the variety of sinusoidal cells was less conspicuous and fewer macrophages were found, but lining cells with large polychromatic nuclei similarly predominated. In man and rodents, progression of the sinusoidal dilatation associated with proliferation of the hepatocytes and sinusoidal cells loosened the parenchymal architecture. Nodules consisting of angiosarcoma cells were noted in man and rodents. Most consisted of spindle-shaped cells, in part in vascular spaces which, however, in part were also lined by nontumorous endothelial cells. In addition, in man, nodules consisted of large polyhedral sarcoma cells with abundant eosinophilic cytoplasm. The center of these nodules usually exhibited hemorrhagic necrosis and these cells then lined bloody cysts. The demonstrated similarity of the evolution in man and rodent strongly supports the extrapolation of observations from experimental animals to man. (58 Refs)

25 AU - Pearson L ; Lindamuth E ; Witte EJ ; Gregg MB
AD - Southeast Distric State Dept. Health, Montgomery County, PA
TI - TRICHLOROETHYLENE EXPOSURE - PENNSYLVANIA.
SI - ICDB/82/21160
SO - MMWR; 30(19):226,231-233 1981
LA - ENG
AB - Effects of a trichloroethylene (TCE) spill in Montgomery County (Pennsylvania) were investigated with respect to well and ground water in the community surrounding the plant where the spill occurred, in air samples in the plant, in urinary excretion of TCE by workers exposed to TCE in the plant. The symptoms of TCE exposure in workers and controls were also examined. Levels of TCE were high in water. Time-weighted-av exposure to TCE vapors decreased below NIOSH recommended levels from February to May. Seven of the nine workers exposed to TCE reported symptoms characteristic of acute TCE exposure. TCE is structurally similar to vinyl chloride, but recent experimental data suggest that TCE

may be a much weaker carcinogen than vinyl chloride. (5 Refs)

26 AU - Byczkowska Z
AD - Klinika Chorob Zawodowych, Instytut Medycyny Pracy w Przemysle Weglowym i Hutniczym, ul. Bieruta 20, 41-200 Sosnowiec, Poland
TI - DATA ON THE CARCINOGENICITY OF VINYL CHLORIDE.
SI - ICDB/82/20073
SO - Pol Tyg Lek; 37(3):95-97 1982
LA - POL
AB - The case of a patient who developed solid hepatic adenocarcinoma after intermittent exposure to vinyl chloride (VC) for 17 yr is reported, and literature on the carcinogenicity of VC is reviewed. Hepatic angiosarcoma is considered a typical tumor developed from the exposure to VC. Other tumors, such as hepatoma, nephroblastoma, adenosarcoma, adenocarcinoma, epidermoid carcinoma, and fibroangioma were also observed in humans or experimental animals following exposure to VC. (35 Refs)

27 AU - Tamburro CH ; Greenberg RA
AD - Department of Medicine, University of Louisville, Louisville, KY
TI - A REVERSE RELATIONSHIP BETWEEN EXPOSURE AND LATENCY IN CHEMICALLY INDUCED LIVER CANCER (MEETING ABSTRACT)
SI - HERN/S2/15894
SO - Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver, February 7-12, 1982, Kowloon, Hong Kong. Asian Pacific Association for the Study of the Liver and International Association for the Study of the Liver 110 pp., 1982.
LA - ENG
AB - It is generally believed that the latency period in cancer development is inversely correlated to the duration of exposure, ie, the longer the exposure, the shorter the latency. Vinyl chloride (VC) induced hepatic angiosarcoma (HA) in humans has allowed study of this relationship in 21 North American cases (NA) and 62 worldwide (WW) reported cases. In all HA cases, VC exposure began between 1941 and 1966; 92% of NA and WW cases had long exposures (LE) (10-33 yrs); 7 cases (8%) had short exposures (SE) (3.5 to 7 yrs). The mean duration in both LE and SE groups was 18.5 yrs with two peaks at 15 and 21 yrs. All (100%) HA cases had greater than 9 yrs latency (9 to 39 yrs) with two peaks occurring at 15 and 25 yrs. Deaths from VC related HA began in 1955, increased to more than one/yr after 1967, peaked in 1976 and have rapidly fallen thereafter. Occurrence peaks were first reached in Canada in 1973 and in USA-1974, France-1976, and Germany-1978. Plant operations began in Canada in 1941; USA in 1939-44; France, 1941-57; and Germany, 1952-60. Reported exposure levels were in ranges of 2000 ppm in the 1940's; 200-500 ppm in 1950's; 50-500 ppm in the early 1960's and 50-250 ppm in the late '60's and early '70's; and about 1 ppm after 1974. Individual latencies showed a direct correlation between total exposure and clinical onset of HA, ie, lower total exposure-shorter latency. This held true for SE and LE groups in both the NA and WW cases. (no Refs)

28 AU - Dietz FK ; Reitz RH ; Watanabe PG ; Gehring PJ
AD - Toxicology Res. Lab., Health and Environmental Sciences, Dow Chemical, 1803 Building, Midland, MI, 48640
TI - TRANSLATION OF PHARMACOKINETIC/BIOCHEMICAL DATA INTO RISK ASSESSMENT.
SI - ICDB/82/19485
SO - Adv Exp Med Biol; 136(partB):1399-1424 1982
LA - ENG
AB - Basic pharmacokinetic principles and biochemical mechanisms which must be considered in order to adequately evaluate the risk of exposure to man from potentially carcinogenic chemicals are reviewed. Dose-independent and dose-dependent pharmacokinetics are discussed. A theoretical model describing the pharmacokinetics of chemical interactions with macromolecules is presented, with emphasis on the importance of knowledge of the dose-related fate of a chemical and its macromolecular target site. Two basic mechanisms responsible for the observation of increased tumor frequencies in the typical animal bioassay are the genetic or genotoxic mechanism and the mechanism through which tumors are produced by a cytotoxic or nongenetic effect. Studies of vinyl chloride (VC) and chloroform illustrate the use of pharmacokinetic and biochemical data of the mechanisms of tumorigenesis to understand the differential carcinogenic response between species with emphasis on risk assessment. With VC, the incidence of hepatic angiosarcomas in humans can be predicted with reasonable accuracy using a probit percentage incidence model. The primary mechanism by which chloroform produces tumors in animal bioassays appears to be recurrent cytotoxicity accompanied by chronic tissue regeneration. The original risk estimation of chloroform was found to be unjustified and overestimated when the species dependent metabolic activation of the compound and the biochemical nature of chloroform-induced tumorigenicity were considered. (38 Refs)

29 AU - Guengerich FP
AD - Dept. Biochemistry, Center Environmental Toxicology, Vanderbilt Univ., Nashville, TN, 37232
TI - METABOLISM OF VINYL HALIDES: IN VITRO STUDIES ON ROLES OF POTENTIAL ACTIVATED METABOLITES.
SI - ICDB/82/19326
SO - Adv Exp Med Biol; 136(partA):685-692 1982
LA - ENG
AB - Mixed-function oxidation of toxic and carcinogenic vinyl halides is thought to be responsible for the mutagenesis and irreversible binding of metabolites observed with these compounds. One suggested reactive metabolite is a 2-haloethylene oxide, which in turn may rearrange to a 2-haloacetaldehyde, both compounds reacting with nucleophilic targets. Studies are reported examining the ability of purified enzymes to specifically destroy the postulated reactive intermediates of vinyl chloride and vinyl bromide in rat liver microsomal systems, utilizing irreversible binding of vinyl halide labels to protein and DNA as indices of

activation. The results are consistent with the view that, in the liver microsomal system, the 2-haloethylene oxides are the species predominantly involved in DNA binding. 2-Haloacetaldehydes, formed from the 2-haloethylene oxides by halogen migration rearrangement, are the primary metabolites binding to protein and glutathione. The 2-haloacetaldehydes, being the more stable intermediates, probably play a significant role in binding to sites outside of the hepatocyte. (22 Refs)

30 AU - Pearson RB
AD - Petrochemicals and Plastics Div., Imperial Chemical Industries Ltd., P.O. Box No. 6, Bessemer Road, Welwyn Garden City, Herts, England
TI - PVC AS A FOOD PACKAGING MATERIAL.
SI - ICDB/82/18527
SO - Food Chem; 8(2):85-96 1982
LA - ENG
AB - Polyvinyl chloride (PVC) polymers used for food packaging, their physical properties, competitiveness with other packaging materials under current market conditions in Britain, their heat stability, their toxicity, and global migration are discussed. Because of the link between vinyl chloride monomer (VCM) and angiosarcoma, the max VCM level in all polymer for food packaging was reduced to 1 ppm; the engineering and chemical modifications that were required to achieve this in PVC for bottle manufacture are briefly described. (no Refs)

31 AU - Chaklin AV ; Gritsiute LA
AD - No affiliation given
TI - CURRENT CONCEPTS OF THE ETIOLOGY AND PATHOGENESIS OF LUNG CANCER.
SI - ICDB/82/17864
SO - Vopr Onkol; 28(2):3-9 1982
LA - RUS
AB - Literature data on the role of smoking and environmental pollutants in the etiology of lung cancer (LC) are reviewed. Epidemiological studies showed the relationship between the smoking and incidence of LC. LC morbidity in 45-64 yr old men increased from 1.4 per 100,000 for nonsmokers to 5.9 for those who smoked 5 cigarettes/day, 13.5 for those who smoked 6-16 cigarettes/day, 29.5 for those who smoked 25-56 cigarettes/day, and 47.4 for those who smoked greater than 56 cigarettes/day. Carcinogenicity of tobacco tar is associated with the presence of polycyclic hydrocarbons, N-nitrosamines, vinyl chloride, phenols, and various co-carcinogens. Recent studies showed the carcinogenic effect of 'passive' smoking. Increased LC morbidity in the regions with intensive chemical industry indicates the co-carcinogenic effect of such air pollutants as sulfur dioxide. Pathogenesis of LC is associated with the history of chronic lung inflammation, tuberculosis, scleroderma, exposure to asbestos, immunologic suppression, and individual activity of aryl hydroxylase. (45 Refs)

32 AU - Greiser E ; Reinl W ; Weber H
AD - (c/o Reinl) Gurlittstrasse 53, D-4000 Dusseldorf, W. Germany
TI - VINYL CHLORIDE EXPOSURE AND MORTALITY AMONG GERMAN CHEMICAL WORKERS IN COMPARISON WITH MORTALITY AMONG NONEXPOSED WORKERS AND PVC MANUFACTURING WORKERS.
SI - ICDB/82/17549
SO - Zentralbl Arbeitsmed Arbeitsschutz Proph; 32(2):44-62 1982
LA - GER
AB - A historical prospective study compared mortality among workers in the German chemical industry. All workers studied were males of German or Austrian nationality. Three cohorts included 7,021 workers exposed to vinyl chloride monomer (VCM) and polyvinyl chloride (PVC), 4,910 chemical workers not exposed to VCM or PVC, and 4,007 workers exposed to PVC. Follow-up rate at the end of the study was approx 90%. The total male population of West Germany for corresponding yr served as controls. Standardized mortality ratios (SMR) showed no 'healthy worker effect' for PVC or VCM/PVC workers. SMR for malignant hepatic tumors was significantly higher than for controls. The increase was dose-dependent. Nonexposed workers showed a small increase in SMR for hepatic malignancies. VCM/PVC worker showed a significantly increased SMR for lymphatic and hematopoietic malignancies. PVC workers showed an increased SMR for malignant brain tumors. VCM/PVC, PVC, and nonexposed workers all showed an increased SMR for ischemic heart disease compared with controls. Because of long latency time for development of malignant tumors and the increasing incidence of hepatic hemangiosarcomas, additional follow-up studies of VCM/PVC workers are urged. (20 Refs)

33 AU - Bishop CS ; Dye A
AD - East Tennessee State Univ., Johnson City, TN, 37614
TI - MICROWAVE HEATING ENHANCES THE MIGRATION OF PLASTICIZERS OUT OF PLASTICS.
SI - ICDB/82/17116
SO - J Environ Health; 44(5):231-235 1982
LA - ENG
AB - The effects of the release of plasticizers from some plastic materials used in conjunction with food in microwave ovens are reviewed. While these plastics are not heated by microwaves, they are heated by conduction of heat from food to a point where the plasticizers may be released; in one study this release amounted to 23% of the total weight. Two commonly used plasticizers are di-2-ethylhexyl phthalate (DEHP), and di-2-ethylhexyl adipate (DEHA). One study showed that mating of male mice given ip one-third of the LD50 of DEHP with untreated virgin females at 12-wk intervals led to a reduction in the number of implantations per pregnancy and litter size. It was inferred that the early fetal deaths and semisterility constitute adverse reproductive and genetic effects of DEHP. Hepatic peroxisome proliferation in association with hepatomegaly were observed in animals treated with DEHP, DEHA, and 2-ethylhexanol but not with adipic acid or diethyl-phthalide. Concerns over other types of changes in

plastics have been expressed in regard to vinyl chloride monomer, polyvinyl chloride, styrene monomer, and acrylonitrile monomer formerly used in soft drink containers. Various other health hazards from plasticizers are discussed. (32 Refs)

34 AU - Desmet VJ
AD - Pathologische ontleedkunde II, Academisch Ziekenhuis Sint-Rafael, B-3000 Leuven, Belgium
TI - DRUG-INDUCED ALTERATIONS OF THE LIVER. HISTOLOGICAL ASPECTS.
SI - ICDB/82/15872
SO - Acta Gastroenterol Belg; 44(9/10):367-374 1981
LA - FRE
AB - Histological characteristics of drug-induced liver disorders are described. Administration of methotrexate for psoriasis may result in hypertrophy and proliferation of liver fibroblasts. Liver irradiation and urethane exposure can cause obliteration of centrolobular veins. Liver adenoma, focal nodular hyperplasia, and hepatocellular carcinoma have been related to the chronic use of oral contraceptives. Exposure to vinyl chloride and ingestion of arsenic compounds has been related to the development of liver angiosarcoma. The differential diagnosis of cholestasis and other disorders, including Hodgkin's and non-Hodgkin's lymphomas is discussed. (8 Refs)

35 AU - Gluszcz M
AD - Klinika Chorob Zawodowych, Instytut Medycyny Pracy, ul. Teresy 8, 90-950 Lodz, Poland
TI - DIFFICULTIES IN THE EARLY DIAGNOSIS OF LIVER DAMAGE DUE TO EXPOSURE TO VINYL CHLORIDE.
SI - ICDB/82/15197
SO - Med Pr; 32(4):277-282 1981
LA - POL
AB - Diagnostic tests were performed in 228 workers exposed occupationally to vinyl chloride (200-1,000 mg/cubic meter) to detect poisoning. Acro-osteolysis was found in 5 cases, vascular disturbances in the extremities in 45. The alanine aminotransferase, aspartic aminotransferase, gamma-glutamyl transpeptidase, alkaline phosphatase, serum cholinesterase, bilirubin and prothrombin levels did not differ significant from those found in 70 unexposed controls. The Bromsulphalein test was positive in 9/50 and moderate hepatomegaly was found in 26/50 exposed workers. (10 Refs)

36 AU - Wronska-Nofer T ; Parke M ; Laurman W
AD - Instytut Medycyny Pracy, ul. Teresy 8, 90-950 Lodz, Poland
TI - BIOCHEMICAL CHANGES IN VINYL CHLORIDE POISONINGS. I. EFFECTS OF DIFFERENT VINYL CHLORIDE EXPOSURE CONDITIONS ON LIPID METABOLISM IN RATS.
SI - ICDB/82/15196
SO - Med Pr; 32(4):247-253 1981
LA - POL
AB - The effect of inhaled vinyl chloride (VC: 50, 500 or 20,000 ppm, exposure time 1-10 mo) on lipid metabolism was studied in male

Wistar rats. Significant increases in the serum triglyceride and phospholipid levels were found after 10-mo exposure to 20,000 ppm. Dose- and exposure time-dependance decreases were seen for cholesterol and especially for the triglyceride levels in liver but not in muscles, aortic wall and connective tissue. The findings indicate that disturbances in lipid metabolism play a minor role in the pathology of VC poisoning. (11 Refs)

37 AU - Suskov II ; Sazonova LA
AD - Inst. General Genetics, Acad. Sciences USSR, Moscow 117333, USSR
TI - CYTOGENETIC EFFECTS OF EPOXY, PHENOLFORMALDEHYDE, AND POLYVINYLCHLORIDE RESINS IN MAN.
SI - ICDB/82/13426
SO - Mutat Res; 104(1-3):137-140 1982
LA - ENG
AB - Cytogenetic effects of synthetic resins were studied in workers exposed to epoxy and polyvinylchloride (PVC) in the manufacture of goods or to phenol and formaldehyde in the production of phenolformaldehyde (PF) resins. Chromosomal aberrations (CA) were analyzed in peripheral lymphocytes from resin workers (av age 39.1 yr, exposure 4 mo-30 yr) and healthy nonexposed controls. Exposure to the synthetic resins and their components was by inhalation and skin exposure. Av concentration of chemical in the air was 6 mg/cubic meter (m3) for vinyl chloride, 1 mg/m3 for epichlorohydrin (a component of epoxy resin), 0.3 mg/m3 for phenol, and 0.5 mg/m3 for formaldehyde. Among controls CA were found in 2.4% of cells; 0.024 aberrant chromosomes (AC)/cell were found; 1.26 breaks/chromosomes were found. The frequency of CA in cells from exposed workers was 5.5% for epoxy resin, 6.1% for PVC, and 5.0% for PF. Significant increases in AC/cell were found for all compounds. A significant increase in chromosomal breaks/cell was found only for PVC. Acentric single and paired chromosomal fragments were the predominant aberration noted, accounting for 90%. Results indicate the need for further study of the hazards of occupational exposure to synthetic resins and components of the resins. (5 Refs)

38 AU - Hallstrom I ; Magnusson J ; Ramel C
AD - Div. Toxicology Genetics, Wallenberg Lab., Univ. Stockholm, Stockholm, Sweden
TI - RELATION BETWEEN THE SOMATIC TOXICITY OF DIMETHYLNITROSAMINE AND A GENETICALLY DETERMINED VARIATION IN THE LEVEL AND INDUCTION OF CYTOCHROME P450 IN DROSOPHILA MELANOGASTER.
SI - ICDB/82/12915
SO - Mutat Res; 92(1/2):161-168 1982
LA - ENG
AB - Enzyme induction and metabolism in Drosophila were studied with the use of somatic toxicity of dimethylnitrosamine (DMN). The activity of cytochrome P450 (P450) in insecticide-resistant Drosophila melanogaster (Hikone R and SHS strains) was higher than the P450 activity of insecticide-sensitive strains. Phenobarbital (PB) induced P450 in the sensitive strains but not in the resistant strains. The toxicity and mutagenicity of DMN

and the uptake of vinyl chloride (VC) were higher in the resistant strains than in the sensitive strains. The correlation between DMN toxicity and the metabolic differences between the insecticide-resistant and sensitive strains was demonstrated by the increased toxicity of DMN after PB pretreatment in the sensitive strains but not in the resistant strains. A dominant gene, responsible for the patterns of VC and presumably DMN metabolism and the non-inducibility of P450 in the Hikone R strain, was located in region 66 cM of chromosome 2, near the vg gene. This gene may be the major gene responsible for the insecticide resistance of the strain. Genetic variation in the mixed function oxidase system associated with insecticide resistance in Hikone R does not apply to the enzyme system as a whole. Benzo(a)pyrene monooxygenase activity and inducibility are the same in the insecticide-sensitive and Hikone R strains of Drosophila. (12 Refs)

39 AU - Hattis D
AD - Center for Policy Alternatives, Massachusetts Inst. Technology, Cambridge, MA, 02139
TI - NEEDS FOR PUBLIC HEALTH INTERVENTION AND NEEDS FOR NEW RESEARCH ON VINYL HALIDES AND THEIR POLYMERS: A PUBLIC POLICY PERSPECTIVE.
SI - ICDB/82/11072
SO - Environ Health Perspect; 41:227-231 1981
LA - ENG
AB - Priorities for regulation and for research on the carcinogenic hazards of vinyl chloride (VC) and the related alkyl and vinyl halides, respiratory system hazards of poly(vinyl chloride), and reproductive hazards of VC, are discussed. The most effective use of limited resources depends on determination of the risk due to exposure under current standards and the likelihood of significant reduction in risk by revision of standards and enforcement. (8 Refs)

40 AU - Apfeldorf R ; Infante PF
AD - Office Carcinogen Identification and Classification, Health Standards, Programs, Occupational Safety and Health Admin. U. S. Dept. Labor, Washington, DC, 20210
TI - REVIEW OF EPIDEMIOLOGIC STUDY RESULTS OF VINYL CHLORIDE-RELATED COMPOUNDS.
SI - ICDB/82/11071
SO - Environ Health Perspect; 41:221-226 1981
LA - ENG
AB - Epidemiologic studies of structural analogs of vinyl chloride (VC) are reviewed. Analogs included epichlorohydrin (ECH), trichloroethylene (TCE), vinylidene chloride (VDC), ethylene dibromide (EDB), perchloroethylene (PCE), and carbon tetrachloride (CCl4). Occupational and industrial uses of the compounds include manufacture of epoxy resins (ECH), copolymers and fibers (VDC), petroleum products (EDB), and pesticides (EDB). Other uses include metal degreasing (CCl4, TCE, and PCE) and dry cleaning (PCE and formerly, TCE and CCl4). Bioassays in experimental animals have demonstrated induction of tumors at

multiple sites by EDB and CCl4, in the respiratory tract by EDB and ECH, and in the liver by VDC, EDB, TCE, PCE, and CCl4. Studies of workers exposed to ECH or dry cleaning solvents suggest an increased risk of lung cancer, but the increase is not significant, possibly due to sample size. Studies of workers exposed to the other compounds have not given positive evidence of carcinogenicity. All studies have been characterized by insensitivity to increases in mortality because of small sample size. In some studies workers were exposed to more than one suspected carcinogen, making interpretation of results difficult. Estimation of qualitative risk to humans due to specific compounds should be based on experimental animal studies rather than on human epidemiological studies. (17 Refs)

41 AU - Chu KC ; Milman HA
AD - NCI, Bethesda, MD, 20205
TI - REVIEW OF EXPERIMENTAL CARCINOGENESIS BY COMPOUNDS RELATED TO VINYL CHLORIDE.
SI - ICDB/82/11070
SO - Environ Health Perspect; 41:211-220 1981
LA - ENG
AB - Results in carcinogenicity studies of vinylidene chloride (VDC), trichloroethylene (TCE), tetrachloroethylene (PCE), 1,2-dichloroethane (DCE), 1,2-dibromoethane (DBE), and epichlorohydrin (EPC), all structural analogs of vinyl chloride (VC), are reviewed. Bioassays of carcinogenicity produced positive results with VDC in Swiss and CD-1 mice and CD and Sprague-Dawley rats. Nonpositive results were obtained with VDC in Fischer rats and B6C3F1 mice. TCE given by gavage or inhalation produced positive results in B6C3F1 mice. Nonpositive results were obtained with TCE in Sprague-Dawley and Osborne-Mendel rats. PCE given by gavage produced positive results in B6C3F1 mice and nonpositive results in Sprague-Dawley and Osborne-Mendel rats. DCE produced positive results in B6C3F1 mice and Osborne-Mendel rats when given by gavage but nonpositive results in Swiss mice and Sprague-Dawley rats when given by inhalation. DBE produced positive results by gavage in B6C3F1 mice and Osborne-Mendel rats. EPC produced positive results in male rats and was an initiator of carcinogenesis when administered sc. Results indicate that compounds thought to act directly without metabolic activation produce tumors at the site of administration, while those requiring activation do not. Important differences were found in response among species and strains. (21 Refs)

42 AU - Vianna NJ ; Brady J ; Harper P
AD - Bureau Environmental Epidemiology, New York State Dept. Health, Tower Building, Empire State Health Plaza, Albany, NY, 12237
TI - ANGIOSARCOMA OF THE LIVER: A SIGNAL LESION OF VINYL CHLORIDE EXPOSURE.
SI - ICDB/82/11069
SO - Environ Health Perspect; 41:207-210 1981
LA - ENG

AB - The association between exposure to vinyl chloride (VCM) and subsequent occurrence of angiosarcoma of the liver (ASL) is reviewed. Although ASL is a rare tumor, some evidence suggests that incidence of ASL is increasing. ASL occurs more frequently among workers occupationally exposed to VCM than among the general population. ASL may also be related to low-level, nonoccupational exposure to VCM. Other disorders possibly associated with exposure to VCM include cancers of the digestive, respiratory, neurologic, and lymphatic systems. (39 Refs)

43 AU - Dimmick WF
AD - Emission Standards and Engineering Div. (MD-13), U. S. Environmental Protection Agency, Research Triangle Park, NC, 27711
TI - EPA PROGRAMS OF VINYL CHLORIDE MONITORING IN AMBIENT AIR.
SI - ICDB/82/11068
SO - Environ Health Perspect; 41:203-206 1981
LA - ENG
AB - Three studies detected vinyl chloride (VC) in the air around plants manufacturing or using VC. An initial monitoring survey detected VC in the air around plants producing poly(vinyl chloride) (PVC). A second program found maximum 24-hr concentrations of 0.32-10.6 ppm in open air; a relationship was found between VC in the air and certain emission excursions. A third study found less VC in the air around PVC fabricating plants than in the air around VC and PVC production plants. (5 Refs)

44 AU - Fabricant JD ; Legator MS
AD - Dept. Preventive Medicine and Community Health, Div. Environmental, Toxicology Univ. Texas Medical Branch, Galveston, TX, 77550
TI - MUTAGENICITY STUDIES OF VINYL CHLORIDE.
SI - ICDB/82/11067
SO - Environ Health Perspect; 41:189-193 1981
LA - ENG
AB - Studies of the mutagenicity of vinyl chloride (VC) in man and test organisms are reviewed. In vitro studies have demonstrated mutagenicity in both prokaryotic and eukaryotic organisms. In vivo studies of cytogenetic effects in animals and humans have demonstrated somatic and germinal mutations. VC hazards and the consequences of mutations are discussed. (26 Refs)

45 AU - Rice JM
AD - Perinatal Carcinogenesis Section, Lab. Comparative Carcinogenesis, NCI, Fort Detrick, Frederick, MD, 21701
TI - PRENATAL SUSCEPTIBILITY TO CARCINOGENESIS BY XENOBIOTIC SUBSTANCES INCLUDING VINYL CHLORIDE.
SI - ICDB/82/11066
SO - Environ Health Perspect; 41:179-188 1981
LA - ENG
AB - Principles of transplacental carcinogenesis and prenatal susceptibility to vinyl chloride (VC) and related compounds are reviewed. Positive results of bioassay for carcinogenicity are

indicated by a dose-related increase in incidence of tumors of one or more organ systems, a dose-related increase in multiplicity of tumors, or a shortening of latency periods. The largest number of carcinogens are small organic molecules, many of which share similar mechanisms of action. Most carcinogens require metabolic activation. The most common metabolic pathway for activation of carcinogens involves mixed-function oxidases. Assays of transplacental carcinogenicity must insure that exposure by other routes, such as through the mother's milk, is excluded. Studies in rats and mice have demonstrated that various compounds, including vinyl chloride (VC), are capable of transplacental carcinogenesis. Studies indicate that the nonhuman primate fetus is susceptible to carcinogens earlier in gestation than the rodent fetus, and different tissues are affected. Analogs of VC would be expected to have activities similar to VC. No evidence has been found suggesting that exposure of males to carcinogens leads to carcinogenesis in offspring of those males. (26 Refs)

46 AU - Lilis R
AD - Environmental Sciences Lab., Dept. Community Medicine, Mount Sinai Sch. Medicine, City Univ. New York, One Gustave Levy Place, New York, NY, 10029
TI - REVIEW OF PULMONARY EFFECTS OF POLY(VINYL CHLORIDE) AND VINYL CHLORIDE EXPOSURE.
SI - ICDB/82/11065
SO - Environ Health Perspect; 41:167-169 1981
LA - ENG
AB - Reported pulmonary effects of poly(vinyl chloride) (PVC) dust are reviewed. Inhalation of PVC dust produces a granulomatous reaction, with inclusion of PVC particles in macrophages and histiocytes and interstitial pulmonary fibrosis (IPF), leading to exertional dyspnea, diffuse micronodular radiographic opacities of the chest, and restrictive pulmonary dysfunction. IPF after exposure to vinyl chloride (VC) may be caused by alteration of proteins by VC and resultant immunologic reactions. VC is associated with increased incidence of lung cancer. (27 Refs)

47 AU - Waxweiler RJ ; Smith AH ; Falk H ; Tyroler HA
AD - Industry-wide Studies Branch, Div. Surveillance, Hazard Evaluations and, Field Studies Natl. Inst. Occupational Safety and Health, 4676 Columbia Parkway, Cincinnati, OH, 45226
TI - EXCESS LUNG CANCER RISK IN A SYNTHETIC CHEMICALS PLANT.
SI - ICDB/82/11064
SO - Environ Health Perspect; 41:159-165 1981
LA - ENG
AB - The occurrence of lung cancer among workers employed at a synthetic chemicals plant at any time during the period 1942-1973 retrospective cohort study included 4,806 males. Of these, 4,174 were alive at the time of the study and 73 were lost to follow-up but assumed to be alive. At the end of the period studied only 30% of the cohort would have been greater than 54 yr old; 63% had the opportunity to achieve 20 yr latency. When all employees were

considereed to be at risk from the start of employment at the plant, the standardized mortality rate (SMR) was significantly elevated for malignant neoplasms of the CNS (SMR 209) and respiratory system (SMR 149). When employees were considered at risk only after 10 yr of employment, results were similar but the SMR was slightly higher. Excess lung cancers were not due solely to exposure to vinyl chloride (VC). A case-comparand study of 27 workers with lung cancer indicated that large-cell undifferentiated type lung cancer (LCLC) occurred more frequently among workers (30%) than among comparands from the community (10%) with lung cancer. Among workers the risk of lung cancer was primarily for LCLC and adenocarcinoma. Analysis of exposure to various chemicals using a serially additive expected dose model indicated poly(vinyl chloride) dust as the most likely etiological agent. The next most likely agent was vinylidene chloride. Latency time peaked at 5-16 yr. (27 Refs)

48 AU - Molina G ; Holmberg B ; Elofsson S ; Holmlund L ; Moosing R
AU - Westerholm P
AD - Occupational Toxicology Unit, Dept. Occupational Medicine, Labor Medicine, Div. Dept. Occupational Safety, Box 100, 26 Stockholm, Sweden
TI - MORTALITY AND CANCER RATES AMONG WORKERS IN THE SWEDISH PVC PROCESSING INDUSTRY.
SI - ICDB/82/11063
SO - Environ Health Perspect; 41:145-151 1981
LA - ENG
AB - Mortality and cancer rates were studied among workers employed in the Swedish polyvinyl chloride (PVC) industry for at least 3 mo in the period 1945-1974. Exposure to vinyl chloride (VC) was classified as high, medium, or low. A total of 2,073 workers were surveyed, of whom 103 could not be followed up. Workers were divided into four study cohorts according to length of exposure and follow-up times. When compared with the national mortality rate, no significant increase was found for the total cohort or for any of the study cohorts. A shift in the cause of death compared with the national average was found. The frequency of myocardial infarction was higher during exposure or within a short time after the end of exposure to VC. The frequency of death due to tumors was apparently higher in individuals with long latency times, but no significant difference was found. Although VC has not been proven a cause of myocardial infarction, the relationship should be considered. The size of two of the study cohorts was too small to permit conclusions regarding the relationship between risk of myocardial infarction and exposure level. (10 Refs)

49 AU - Jones JH
AD - Div. Surveillance, Hazard Evaluations and Field Studies, Natl. Inst. Occupational Health and Safety, 4676 Columbia Parkway, Cincinnati, OH, 45226
TI - WORKER EXPOSURE TO VINYL CHLORIDE AND POLY(VINYL CHLORIDE).
SI - ICDB/82/11061
SO - Environ Health Perspect; 41:129-136 1981
LA - ENG
AB - Industrial hygiene studies were conducted among workers at three vinyl chloride (VC) monomer (VCM) plants, three vinyl chloride polymerization (VCP) plants, and seven polyvinyl chloride (PVC) fabrication plants. Exposure to VC was highest among VCP workers and lowest among PVC workers. One job category at VCM plants had exposures greater than 1 ppm. The highest av exposure was 22 ppm. Later studies have shown undetectable levels of VC, although in several cases levels greater than 1ppm were found. (36 Refs)

50 AU - Baxter PJ
AD - Chronic Diseases Div., Special Studies Branch, Center Disease Control, Atlanta, GA, 30333
TI - THE BRITISH HEPATIC ANGIOSARCOMA REGISTER.
SI - ICDB/82/11060
SO - Environ Health Perspect; 41:115-116 1981
LA - ENG
AB - A register has been established to record cases of hepatic angiosarcoma (HAS) in Britain. Thirty-five cases of HAS in patients dying during the period 1963-1977 have been confirmed. HAS was related to exposure to vinyl chloride monomer (VCM) in two cases and to ia administration of Thorotrast (a colloidal suspension of thorium dioxide) in eight cases. Two additional cases associated with exposure to VCM were confirmed in 1978-1979. (7 Refs)

51 AU - Falk H ; Herbert J ; Crowley S ; Ishak KG ; Thomas LB ; Popper H
AU - Caldwell GG
AD - Chronic Diseases Div., Center Environmental Health, Centers Disease, Control, Public Health Service U. S. Dept. Health and Human Services, Atlanta, GA, 30333
TI - EPIDEMIOLOGY OF HEPATIC ANGIOSARCOMA IN THE UNITED STATES: 1964-1974.
SI - ICDB/82/11059
SO - Environ Health Perspect; 41:107-113 1981
LA - ENG
AB - The occurrence of hepatic angiosarcoma (HAS) in the United States was studied for the period 1964-1974. Death certificates were reviewed in 22,432 cases of death due to liver tumors. Based on examination of medical records and pathological specimens, 168 cases of HAS were confirmed. Of cases identified as HAS on death certificates, only 42% were confirmed as HAS by other evidence; 50% were confirmed as not HAS. Only 23% of confirmed cases of HAS would have been identified by a search of death certificates alone. Inadequacies in epidemiological studies are indicated. HAS

occurred predominantly in men (male:female ratio 3:1) and more frequently in the younger age groups. The mean age was 50.1 yr for women and 57.9 yr for men. Of 127 men with HAS, 12 had been exposed to vinyl chloride (VC), 15 to Thorotrast (TT), 4 to inorganic arsenic (As), and 3 to androgenic-anabolic steroids (AAS); 93 cases were classified as idiopathic. Of 41 women with HAS, 5 had been exposed to TT, 2 to As, and 1 to AAS; 33 cases were classified as idiopathic. A relationship between HAS and VC, TT, or AAS was more common in the latter part of the study period, probably due to recent introduction of VC and AAS and a long latency period for TT. The mortality rate for HAS was 0.75 cases/10(7) population/yr. The mortality rate was apparently higher in industrialized areas of the Northeast and Midwest and lower in farming states and the South; differences in rates for different areas may have been due to reporting methods rather than to actual differences in occurrence. Four agents have been identified as probable causative factors in HAS, but 75% of cases are of uncertain etiology. (28 Refs)

52 AU - Cooper WC
AD - 2150 Shattuck Ave., Suite 401, Berkeley, CA, 94704
TI - EPIDEMIOLOGIC STUDY OF VINYL CHLORIDE WORKERS: MORTALITY THROUGH DECEMBER 31, 1972.
SI - ICOB/82/11058
SO - Environ Health Perspect; 41:101-106 1981
LA - ENG
AB - A survey of the vital status of 9,677 men working for at least 1 yr with probable exposure to vinyl chloride monomer (VCM) showed that 707 workers had died. Standardized mortality ratios (SMR) calculated for 699 deaths were 89 for all causes and 104 for malignancies. The only types of malignancy found in significant excess were neoplasms of the brain and other parts of the nervous system: 5.9 deaths were expected but 12 occurred, for an adjusted SMR of 203. No significant differences were found among workers with less than 20 yr, greater than 20 yr, or greater than 25 yr exposure to VCM. (6 Refs)

53 AU - Weber H ; Reinl W ; Greiser E
AD - Staatlicher Gewerbearzt, Dusseldorf, W. Germany
TI - GERMAN INVESTIGATIONS ON MORBIDITY AND MORTALITY OF WORKERS EXPOSED TO VINYL CHLORIDE.
SI - ICOB/82/11057
SO - Environ Health Perspect; 41:95-99 1981
LA - ENG
AB - Morbidity and mortality among workers of German or Austrian nationality exposed to vinyl chloride monomer (VCM) were studied. Standardized mortality ratios (SMR) were calculated. SMR for workers exposed to VCM were compared with those for the West German male population, chemical workers not exposed to VCM, and workers exposed to polyvinyl chloride (PVC). Cause of death could not be determined in 7.3-13.1% of cases. Data from VCM and PCV workers did not show a 'healthy worker' effect. Among VCM workers, SMR were elevated for malignancies of the lymphatic and

hematopoietic systems and for malignancies of the gastrointestinal (GI) tract. The increase in SMR for GI cancers was due to an increase in deaths due to liver cancers. SMR for liver cancers was also somewhat elevated for workers not exposed to VCM; cause of the elevation was uncertain. SMR for ischemic heart disease was elevated for all three groups of workers. SMR for liver cancers increased with time of exposure to VCM, suggesting a time-response relationship. A dose-response relationship could not be established due to lack of dose determinations. SMR for cancers in general and for liver cancers were particularly high for men 35-44 yr old. A study of morbidit indicated 269 cases of suspected occupational disease among 6,50 workers in VCM or PVC production and 42,800 workers in PVC processing. (2 Refs)

54 AU - Infante PF
AD - Office Carcinogen Identification and Classification, Health Standards, Program, Occupational Safety and Health Admin. U. S. Dept. Labor, Washington, DC, 20210
TI - OBSERVATIONS OF THE SITE-SPECIFIC CARCINOGENICITY OF VINYL CHLORIDE TO HUMANS.
SI - ICDB/82/11056
SO - Environ Health Perspect; 41:89-94 1981
LA - ENG
AB - Studies of site-specific carcinogenicity of vinyl chloride (VC) are reviewed. Problems encountered included relative insensitivity to carcinogenic response at low risk sites due to small sample size, and characteristics of method and design that prevent adequate interpretation of results. Restriction of disease definition resulted in obscuring some sites that might otherwise have shown significant excess risk. Four of eight studies indicated a significant risk of liver cancer following exposure to VC, although the liver had been confirmed as a site of VC-carcinogenesis by other studies. Problems with studies of liver cancer included insufficient exposure and observation times. Some studies classify liver cancer with other cancers of the digestive tract. Overall data from at least one study of cancers of the digestive tract indicate a reduction in mortality among exposed workers. An excess of mortality due to CNS cancers was indicated by five of eight studies. Some studies classified CNS cancers with nonspecific 'other' categories. Data for lung cancer mortality suggest a significant increase in risk for workers exposed to VC. Data for cancers of the lymphatic and hematopoietic systems are suggestive but not conclusive. Overall data indicates that the carcinogenic effect of VC is not limited to the liver. (12 Refs)

55 AU - Maltoni C ; Lodi P
AD - Inst. Oncology, Bologna, Italy
TI - RESULTS OF SPUTUM CYTOLOGY AMONG WORKERS EXPOSED TO VINYL CHLORIDE MONOMER AND TO POLY(VINYL CHLORIDE).
SI - ICDB/82/11055
SO - Environ Health Perspect; 41:85-88 1981
LA - ENG
AB - Systematic cytological examinations of sputum were performed in 3380 workers exposed to vinyl chloride monomer (VC), some of whom were also exposed to poly(vinyl chloride) (PVC). Results were compared with those from 2,287 workers in other industries with different potential risks. VC-PVC workers had a higher incidence of cellular abnormalities and dysplasias in the respiratory tract than other workers. Results suggest a risk of upper respiratory oncogenesis among VC-PVC workers. (5 Refs)

56 AU - Mehir RM ; McNamara BP ; McLaughlin J ; Williqan DA ; Bierbower
AU - Hardisty JF
AD - U. S. Consumer Product Safety Commission, Westwood Towers Building, Room 738, 5401 West Blvd., Washington, DC, 20207
TI - CANCER INDUCTION FOLLOWING SINGLE AND MULTIPLE EXPOSURES TO A CONSTANT AMOUNT OF VINYL CHLORIDE MONOMER.
SI - ICDB/82/11054
SO - Environ Health Perspect; 41:63-72 1981
LA - ENG
AB - The effects of total dose and frequency of exposure on carcinogenesis of vinyl chloride monomer (VCM) were studied in Fischer 344 and Sprague-Dawley rats and A/J and ICR mice. Fischer rats and ICR mice were exposed to a single dose of 50, 500, 5,000, or 50,000 ppm VC for 1 hr. Fischer rats and A/J mice were exposed 10x to 500 ppm VCM (1 hr/day, 5 day/wk for 2 wk) or 100x to 50 ppm (1 hr/day, 5 days/wk for 20 wk). Sprague-Dawley rats were exposed to 50-500 ppm VC (1 hr/day, 5 days/wk for 10 wk). All test animals were observed until sacrifice (18-24 mo). Animals were killed when moribund or on schedule. Significant toxic effects were observed only at 50,000 ppm. VCM produced dose-related increases in the frequency of pulmonary adenomas and carcinomas in mice at concentrations of 5,000 and 50,000 ppm. Multiple exposures of A/J mice to 500 ppm produced significant increases in occurrence of pulmonary adenomas and carcinomas. Multiple exposures to 50 ppm did not produce significant increases in occurrence of the tumors. Carcinogenic effects were not observed in rats at the total VCM doses used. Results indicate that carcinogenesis depends on total dose but concentration may be the most critical factor in short-term exposure. Single exposure required at least 5,000 ppm-hr in mice or 50,000 ppm-hr in rats for carcinogenesis. Mice were more sensitive than rats to VCM. (10 Refs)

57 AU - Radike MJ ; Stemmer KL ; Bingham E
AD - Dept. Environmental Health, Kettering Lab., Univ. Cincinnati Medical Center, 3223 Eden Ave., Cincinnati, OH, 45267
TI - EFFECT OF ETHANOL ON VINYL CHLORIDE CARCINOGENESIS.
SI - ICDB/82/11053
SO - Environ Health Perspect; 41:59-62 1981
LA - ENG
AB - The potential cocarcinogenicity of ethanol with vinyl chloride (VC) was studied in male Sprague-Dawley rats. A total of 320 rats (80 rats in each of four groups) were studied: Group 1 was exposed to VC (600 ppm, 4 hr/day, 5 days/wk for 1 yr), Group 2 was exposed to VC and ethanol (5% in water, beginning 4 wk before the start of VC exposure and continuing for life), Group 3 was exposed only to ethanol, and Group 4 was exposed only to filtered air. At 18 mo rats exposed to VC showed an av weight loss of approx 9%. At 18 mo the survival rate was 40% for Group 1, 18% for Group 2, 73% for Group 3, and 70% for Group 4. Angiosarcomas were found in 23% of Group 1, 50% of Group 2, and 0% of Groups 3 and 4. Hepatocellular carcinomas were found in 44% of Group 1, 60% of Group 2, 10% of Group 3, and 0% of Group 4. Lymphosarcomas were found in all groups but most frequently in Group 2. Endocrine tumors were found in 57 rats in Group 3, compared with 29 in Group 1, 30 in Group 2, and 8 in Group 4. Some rats developed more than one angiosarcoma or carcinoma. Results indicate that ethanol has a strong cocarcinogenic effect in rats exposed to VC. (8 Refs)

58 AU - Groth DH ; Coate WB ; Ulland BM ; Hornung RW
AD - Div. Biomedical and Behavioral Science, Natl. Inst. Occupational Safety and Health
TI - EFFECTS OF AGING ON THE INDUCTION OF ANGIOSARCOMA.
SI - ICDB/82/11052
SO - Environ Health Perspect; 41:53-57 1981
LA - ENG
AB - The effects of aging on chemical induction of angiosarcoma were studied in adult Sprague-Dawley albino rats. In each of four age groups (6, 18, 32, and 52 wk old at the start of exposure), 110-128 male rats and an equal number of female rats were exposed to vinyl chloride (VC: 948 ppm, 7 hr/day, 5 days/wk for a mean duration of 24.5 wk). Equal numbers of controls were kept under identical conditions but were not exposed to VC. Rats exposed to VC did not show any significant differences in mean hematological or clinical chemistry measurements at interim sacrifice times when compared with controls. Angiosarcomas were found in 28/370 exposed males and 50/387 exposed females; among controls only one sc angiosarcoma was found. Angiosarcomas occurred more frequently with increasing age at the start of exposure. Among male rats killed at unscheduled times, the occurrence rates were 0% for 6-wk-, 0% for 17-wk-, 6.7% for 32-wk-, and 24% for 52-wk-old rats. The corresponding rates for female rats were 5.3%, 15%, 47%, and 20%. Times between start of exposure and first appearance of tumors were shorter in older rats than in younger

rats. Most of the angiosarcomas in exposed rat were highly anaplastic primary tumors of the liver with pulmonary metastases. Results indicate that older rats and female rats are more susceptible to induction of angiosarcomas by VC than younger rats and female rats, respectively. (3 Refs)

59 AU - Suzuki Y
AD - Environmental Sciences Lab., Dept. Community Medicine, Mount Sinai, Sch. Medicine City Univ. New York, One Gustave Levy Place, New York, NY, 10029
TI - NEOPLASTIC AND NONNEOPLASTIC EFFECTS OF VINYL CHLORIDE IN MOUSE LUNG.
SI - ICDB/82/11051
SO - Environ Health Perspect; 41:31-52 1981
LA - ENG
AB - Carcinogenicity of vinyl chloride (VC) was studied in the lungs of CDI Charles River white strain mice. Of 27 mice, 6 were exposed to VC (2,500 or 6,000 ppm) for 5 hr/day, 5 days/wk for 5 mo and killed after a 6-day period without treatment. Thirteen mice were exposed to VC (2,500 or 6,000 ppm) for 6 mo and killed 2 days after the end of treatment. Eight mice were exposed to VC (2,500 or 6,000 ppm) for 6 mo and killed after a 37-day recovery period. The effects of lower doses (0, 1, 10, or 100 ppm, 5 hr/day, 5 days/wk for 4 wk) were studied in 120 mice. Pulmonary tumors were found in 26/27 mice treated with the higher doses. Tumors were multiple and either tubulo-papillary or adenomatous. No metastases were found. Electron microscopy showed short microvilli, tight junctions between adjacent cells, osmiophilic lamellar bodies, large irregular mitochondria, well-developed Golgi complexes, continuous or discontinuous basement membranes, occasional sequestration of crystalloids, and lack of cilia and secretory granules. Tumors were classified as alveologenic, possibly developing from hyperplastic Type II alveolar epithelium. Nonneoplastic effects included proliferation and hypertrophy of bronchiolar cells, abnormal mitochondria, and proliferation of rough endoplasmic reticulum. Low doses of VC produced tumors in 5/9 mice at 100 ppm, 2/9 at 10 ppm, 1/9 at 1 ppm, and 0/10 at 0 ppm. Results indicate that VC induces pulmonary tumors in mice in a dose-related fashion; mouse lung is a sensitive indicator of VC carcinogenicity. (52 Refs)

60 AU - Maltoni C ; Lefemine G ; Ciliberti A ; Cotti G ; Carretti D
AD - Inst. Oncology and Tumor Center, Bologna, Italy
TI - CARCINOGENICITY BIOASSAYS OF VINYL CHLORIDE MONOMER: A MODEL OF RISK ASSESSMENT ON AN EXPERIMENTAL BASIS.
SI - ICDB/82/11050
SO - Environ Health Perspect; 41:3-29 1981
LA - ENG
AB - Bioassays of vinyl chloride (VC) monomer were performed to assess the carcinogenicity, types and locations of tumors induced, the effects of various modes of administration (particulary those simulating potential human exposure), and the level of risk. VC was administered to Sprague-Dawley rats, Wistar rats, Swiss mice,

and golden hamsters. Methods of administration included inhalation (14 dose rates: 1-30,000 ppm, 4 hr/day, 5x/wk), ingestion (6 dose rates: 0.03-50 mg/kg, 5x/wk for 52 wk), ip injection (4.25 mg 1x or 2, 3, or 4x at 2-wk intervals), and sc injection (4.25 mg 1x). VC was carcinogenic in all animal systems tested and was a multipotential carcinogen, causing various types of tumors at various sites. Some tumor types occurred in all species, while some occurred only in one species. Carcinogenesis was induced by inhalation, ingestion, and possibly injection. Response was strongly affected by duration and schedule of administration and strain and sex of the animals studied. VC was carcinogenic even at low doses and produced tumors in embryos after crossing the placenta. (13 Refs)

61 AU - Wynder EL
AD - American Health Foundation, 320 East 43rd St., New York, NY, 10017
TI - THE ETIOLOGY, EPIDEMIOLOGY, AND PREVENTION OF LUNG CANCER.
SI - ICDB/82/10810
SO - Semin Respir Med; 3(3):135-139 1982
LA - ENG
AB - The risk of lung cancer increases proportionally with the number of cigarettes smoked/day and the number of yr smoked. Smoking is the primary cause of lung cancer. Epidemiologic studies have suggested that risk of lung cancer decreases with reductions in the amount of tar in cigarettes smoked. Occupational exposure to asbestos, uranium, arsenic, coal products, bischloromethyl ether, vinyl chloride, nickel, chromium, iron oxide, and mustard gas is also associated with an increased risk of lung cancer. Some occupational exposures work synergistically with tobacco smoke. The higher rate of lung cancer in cities than rural areas can be explained by higher frequency of smoking, more occupational exposure to carcinogens, and higher reporting of lung cancer. The relationship between passive inhalation of cigarette smoke and lung cancer is unproven. Lung cancer can be prevented by preventing smoking in children, the cessation of smoking by adults, and by developing less harmful cigarettes. (15 Refs)

62 AU - Filatova VS ; Antoniuzhenko VA ; Smulevich VB ; Fedotova IV
AU - Kryzhanovskaia NA ; Bochkareva TV ; Goriacheva LA ; Bul'bulian MA
AD - Res. Inst. Industrial Hygiene and Occupational Diseases, Gorky, USSR
TI - CARCINOGENIC ACTIVITY OF VINYL CHLORIDE (DATA OF CLINICO-HYGIENIC AND EPIDEMIOLOGICAL STUDY).
SI - ICDB/82/10045
SO - Gig Tr Prof Zabol; (1):28-31 1982
LA - RUS
AB - Incidence of malignant tumors was studied in workers who had an occupational exposure to vinyl chloride (VC) and polyvinyl chloride (PVC). Group 1 was exposed to VC at greater than 300 mg/cubic meter (m3), Group 2 was exposed to VC in concentrations of 30-300 mg/m3, and Group 3 was exposed to VC in concentrations of less than 30 mg/m3. Analysis of cancer morbidity showed that 31.7% had stomach cancer, 26.9% had lung cancer and 14.3% had

lymphatic and hematological malignancies. Cancer mortality index in Groups 1, 2, and 3 was 1.4, 1.3, and 0.6, respectively. Cancer mortality depended upon the duration of exposure. (15 Refs)

63 AU - International Cancer Research Data Bank National Cancer Institute
AD - International Cancer Research Data Bank, NCI, NIH, Westwood Bldg. 10A18, 5333 Westbard Ave., Bethesda, MD, 20205
TI - THE CARCINOGENICITY OF VINYL CHLORIDE AND RELATED COMPOUNDS (ONCOLOGY OVERVIEW).
SI - ICDB/80/78614
SO - The Carcinogenicity of Vinyl Chloride and Related Compounds (Oncology Overview). Van Duuren BL, ed. This Title is Available Through National Technical Information Service, Springfield, Va, as PB80-922904, 85 pp., 1980.
LA - ENG
AB - ONCOLOGY OVERVIEWs are retrospective bibliographies with abstracts, published by the International Cancer Research Data Bank Program of the NCI. Each issue contains 100-500 selected abstracts on topics of high interest to cancer researchers, as well as an editorial commentary, subject and author indexes. This ONCOLOGY OVERVIEW on the carcinogenicity of vinyl chloride and related compounds contains selected abstracts of articles published mainly during 1975-79. It includes articles on the carcinogenicity, teratogenicity, and mutagenicity of vinyl chloride and related compounds including chloroprene, vinylidene chloride, trichloroethylene and dichloroethylene, and other analogous halogenated hydrocarbons. Studies of the chemistry and analysis, pharmacokinetics, biological effects in animals and humans, chemical structure and biological activity of vinyl chloride and its analogs are included. Also included are epidemiological investigations and discussions of public health issues, occupational safety and regulations. Studies of halogenated aromatics and of anesthetics are specifically excluded from this OVERVIEW.

64 AU - Bergman K
AD - Toxicology Lab., Natl. Food Admin., Box 622, S-751 26 Uppsala, Sweden
TI - REACTIONS OF VINYL CHLORIDE WITH RNA AND DNA OF VARIOUS MOUSE TISSUES IN VIVO.
SI - ICDB/82/03816
SO - Arch Toxicol; 49(2):117-129 1982
LA - ENG
AB - The irreversible binding of 14C-vinyl chloride metabolites to RNA and DNA of mouse brain, lung, liver, kidney, spleen, pancreas, and testes after a single ip injection has been studied. Hydrolysates of nucleic acids from selected organs were separated on Aminex A6 for quantitation of alkylation products. Radioactivity in nucleic acids was registered in all of the studied organs with the exception of brain. RNA from spleen, pancreas and liver, and DNA from spleen and liver contained the highest amounts of radioactivity. In nucleic acids from spleen and pancreas, both organs of high metabolic activity, the entire

radioactivity was found metabolically incorporated as Cl-fragments. In RNA of kidney and liver, a large part of the radioactivity was also present as incorporated Cl-fragments, but 3,N4-ethenocytidine (in kidney) as well as 1,N6-ethenoadenosine and 1,N6-ethenoadenine (in kidney and liver) were identified as alkylation products. In liver DNA, incorporation of Cl-fragments was insignificant, indicating different interactions of vinyl chloride metabolites (Cl-fragments and alkylating products) with RNA and DNA. The elution profiles of radioactivity in hydrolysates of liver DNA were dominated by an alkylation product of unknown structure (probably a derivative of deoxyguanosine). Possibly, 1,N6-ethenodeoxyadenosine and 1,N6-ethenoadenine were also present in liver DNA. The results are consistent with the ability of viny chloride to act as a multipotent carcinogen by alkylation of DNA in several tissues. (Author abstract) (45 Refs)

65 AU - Zimmerman HJ
AD - George Washington Univ. Sch. Medicine, Washington, DC
TI - JAUNDICE: DRUGS THAT CAN CAUSE ICTERUS.
SI - ICDB/82/08723
SO - Consultant; 22(2):76-79,83-85,89 1982
LA - ENG
AB - Drug-induced jaundice which results from direct injury to hepatocytes is discussed. Such injury is reviewed with a discussion of mechanisms of action, effecting drugs according to therapeutic application, and treatment of drug-induced lesions. Many drugs used in oncotherapy produce steatosis, necrosis, or degeneration of cells or hepatocanalicular cholestasis. Benign liver cell adenoma, malignant hepatocellular carcinoma, and hepatic angiosarcoma are caused by such drugs as anabolic and contraceptive steroids, thorotrast, vinyl chloride, and inorganic arsenic. (3 Refs)

66 AU - Clemmesen J
AD - (c/o P. H. Lohman), Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
TI - MUTAGENICITY AND TERATOGENICITY OF VINYL CHLORIDE MONOMER (VCM): EPIDEMIOLOGICAL EVIDENCE.
SI - ICDB/82/08603
SO - Mutat Res; 93(1):97-100 1982
LA - ENG
AB - While there is little evidence to attribute isolated cases of hepatic angiosarcoma to to vinyl chloride monomer (VCM) exposure, it would be important if mutagenic or teratogenic effects of VCM could be demonstrated in the surroundings of factories or in the domestic environment of workers. In support of this thesis, a review of epidemiological studies was made to find supportive evidence in the form of excess infant deaths or birth defects. Although excess birth defects were found in an Ohio study, these could not be attributed to polyvinyl chloride (PVC) plants due to the nonuniform distribution within communities having plants and those without them up to 12 miles away. Although excess CNS-malformation in newborns was found in another study, in one

of the towns with two PVC plants, none of the parents of involved patients worked at the plants. An attempt to determine infant death rates from pregnancies initiated before and after exposure of the same fathers to VCM or PVC fabrication have been confused by a number of factors. It was concluded that none of these studies were supportive of VCM or PVC plants being responsible for isolated hepatic angiosarcoma, excess infant death rates, or excess birth defects. (8 Refs)

67 AU - Bolt HM ; Laib RJ ; Filser JG
AD - Pharmakologisches Institut, Abteilung Toxikologie, Johannes Gutenberg-Universitat Mainz, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany
TI - REACTIVE METABOLITES AND CARCINOGENICITY OF HALOGENATED ETHYLENES.
SI - ICDB/82/06816
SO - Biochem Pharmacol; 31(1):1-4 1982
LA - ENG
AB - Mutagenicity and carcinogenicity of halogenated ethylenes (HE) are reviewed with special emphasis on the role of molecular rearrangement in metabolic detoxication. Comparison of the data on the formation of hepatic preneoplastic foci after exposure of young Wistar rats to HE with the metabolic data showed significant reduction of the wide range of oncogenic activities when the preneoplastic effects were related to the amount of HE metabolites produced after 400 hr of exposure. It is suggested that monochlorooxirane (the epoxide of vinyl chloride) represents an optimum between stability and reactivity to reach the DNA target and react with it. (47 Refs)

68 AU - Popper H ; Selikoff IJ
AD - Stratton Lab., Mount Sinai Sch. Medicine, City Univ. New York, 10 East 102nd St., New York, NY, 10029
TI - CLASSICAL SYNDROMES IN OCCUPATIONAL MEDICINE: PATHOLOGICAL LESSONS FROM VINYL CHLORIDE ANGIOSARCOMA.
SI - ICDB/82/08810
SO - Am J Industr Med; 2(2):187-196 1981
LA - ENG
AB - Similarities in the evolution of the various stages of vinyl chloride (VC)-induced hepatic lesions in man and experimental animals are discussed. The initial lesion in man and rodents is focal proliferation of hepatocytes which show variations in size and appearance of nuclei. Increase of perisinusoidal collagen fibrils and of fat-storing interstitial cells, precursors of fibroblasts, is present. Silver impregnation visualizes the increase of reticulin fibers in circumscribed zones. The precursor lesions do not exclude the simultaneous presence of fully developed angiosarcoma (AS) in other parts of the liver. Diagnostic follow-up by radionuclide scanning, angiography, and subsequent confirmation by open liver biopsy are indicated. The proliferation of sinusoidal cells becomes more conspicuous in both man and animals, and cells with hyperchromatic spindle-shaped nuclei gradually exceed the other sinusoidal cells in number. Intralobular AS is always multicentric in rodents.

Exposure of newborn rats produced mainly hepatocellular carcinoma. Trabecular AS is the more frequent form. Increased connective tissue and AS cells which invade the cords are present leading to atrophy and disappearance of hepatocytes. Solid nodules of AS often form. In humans all forms of AS are almost always multicentric discouraging surgical intervention even at early stages. VC produces a well defined histological sequence in animals and man, leading to control of exposure and avoidance of additional disease. (36 Refs)

69 AU - Brenner EA ; Manchester KL ; Webster I ; Cantrell AC
AD - National Centre for Occupational Health, P.O. 4788, Johannesburg, South Africa
TI - ATTEMPTS TO DEMONSTRATE SHORT-TERM METABOLIC EFFECTS OF VINYL CHLORIDE IN NORMAL RAT LIVER.
SI - ICDB/82/08606
SO - Am J Industr Med; 2(2):153-159 1981
LA - ENG
AB - Effects of vinyl chloride monomer (VCM) and one of the metabolites, chloroacetaldehyde, on cell metabolism were assessed measuring adenine nucleotide concentrations and resting transmembrane potentials. Results indicated that VCM does not alter general cell metabolism but could act on specific intracellular target. (16 Refs)

70 AU - Suzuki Y
AD - Environmental Sciences Lab., Mount Sinai Sch. Medicine, One Gustav Levy Place, New York, NY, 10029
TI - ELECTRON MICROSCOPIC OBSERVATIONS OF HEPATIC AND SUBCUTANEOUS HEMANGIOSARCOMAS INDUCED IN MICE EXPOSED TO VINYL CHLORIDE MONOMER.
SI - ICDB/82/08804
SO - Am J Industr Med; 2(2):103-117 1981
LA - ENG
AB - Neoplastic effects of vinyl chloride was studied in mice in short exposure (4 wk) to low doses (1, 10, 100, 300, and 600 ppm). A mouse of the 10 ppm group developed a subcutaneous hemangiosarcoma, 29 wk after exposure. Histologically the tumor was localized in the subcutaneous connective tissue of the ear, and formed blood channels that appeared to be freely communicated. Neoplastic cells (NC) that directly lined the blood cavities were generally attenuated. Focal necrosis, hemorrhage, and hemosiderin deposition were observed. Ultrastructure of the attenuated NC was similar to that of capillary endothelium in the connective tissue. A mouse of the 600 ppm group developed an hepatic hemangiosarcoma approx 65 wk after exposure. The tumor was found on the surface of the lobe of the liver, and in addition, multiple pulmonary tumors were observed. The hepatic tumor showed formation of cystic blood channels, and the stroma of the tumor was frequently sclerotic. Neoplastic tissue contained degenerated hepatic parenchyma. NC lining the blood cavity were attenuated compared with normal sinusoidal endothelium. Pericyte-like cells were characterized by the

presence of pinocytotic vesicles and dense bodies beneath the cell membrane. Under normal conditions the pericyte does not exist in Disse's space of the mouse. Alveologenic tumors were induced at high rate in mice 12 wk and longer after exposure; 23/24 mice in the 600 ppm group, 12/19 in the 300 ppm, 7/16 in the 100 ppm, 3/20 in the 10 ppm group, and in 2/38 control group. (28 Refs)

71 AU - Sal'nikova LS ; Vorontsov RS
AD - Inst. Industrial Hygiene and Occupational Diseases, Moscow, USSR
TI - LONG-TERM EFFECTS OF VINYL CHLORIDE ON EMBRYOGENESIS.
SI - ICOB/82/08416
SO - Gig Tr Prof Zabol; (12):56 1981
LA - RUS
AB - Potential transplacental carcinogenic effect of vinyl chloride (VC) was studied in SHK mice. Pregnant females were subjected to inhalation exposure to VC at 35.3 and 4.8 mg/cubic meter. The offspring were followed up for 1-1.5 yr. The antenatal exposure to VC did not increase the incidence of malignant tumors. (6 Refs)

72 AU - Emmerich KH ; Norpoth K
AD - Inst. Pathology, Univ. Munster, Domagkstr. 17, D-4400 Munster, W. Germany
TI - MALIGNANT TUMORS AFTER CHRONIC EXPOSURE TO VINYL CHLORIDE.
SI - ICOB/82/05131
SO - J Cancer Res Clin Oncol; 102(1):1-11 1981
LA - ENG
AB - Correlations between exposure to vinyl chloride and the development of malignant tumors in the liver have been known since 1974 and have been confirmed by many an experimental investigation. Based on the evaluation of mortality statistics from nine different countries an increased incidence of malignant tumors of the lung, the gastrointestinal tract, and the central nervous system (CNS), and of malignant lymphomas is documented in connection with exposure to vinyl chloride. Statistically significant increases, however, are only found in the incidence of malignant liver tumors. Metabolism and toxicology of vinyl chloride are discussed in detail. (Author abstract) (78 Refs)

73 AU - von Daniken A ; Friederich U ; Lutz WK ; Schlatter C
AD - Inst. Toxicology, Swiss Federal Inst. Technology, CH-8603 Schwerzenbach, Switzerland
TI - TESTS FOR MUTAGENICITY IN SALMONELLA AND COVALENT BINDING TO DNA AND PROTEIN IN THE RAT OF THE RIOT CONTROL AGENT O-CHLOROBENZYLIDENE MALONONITRILE (CS).
SI - ICOB/82/04758
SO - Arch Toxicol; 49(1):15-27 1981
LA - ENG
AB - The aim of this study was to determine whether o-chlorobenzylidene malononitrile (CS) exhibits any genotoxic activity towards Salmonella or mammalian DNA in vivo. CS was synthesized with a (14C)-label at the benzylic carbon atom. It was administered ip at a dose level of 13 mg/kg (1 mCi/kg) to

young adult male rats. Liver and kidney DNA was isolated after 8, 25, and 75 hr. The radioactivity was at (liver, 8 and 75 hr) or below (all other samples) the limit of detection of 3 dpm. Therefore, a possible binding of CS to DNA is at least 10(5) times lower than that of the strong hepatocarcinogen aflatoxin B1, and 4,000x lower than that of vinyl chloride. In contrast to this lack of DNA binding, but in agreement with the chemical reactivity of CS, a binding to nuclear proteins could be detected with specific activities ranging between 50 and 121 dpm/mg for liver and between 3 and 41 dpm/mg for kidney. Protein binding could well be responsible for its pronounced cytotoxic effects. CS was also tested in the Ames Salmonella/microsome assay. Strains TA 1535, TA 1537, TA 1538, TA 98, and TA 100 were used with or without pre-incubation. Only with strain TA 100 and only without pre-incubation, a doubling of the number of revertants was detectable at the highest dose levels used, 1,000 and 2,000 ug CS per plate. With pre-incubation of TA 100 with CS, a slight increase of the number of revertants was seen at 100 and 500 ug per plate, and a subsequent fall below control values at 1,000 ug. A check for the number of surviving bacteria revealed a strong bacteriotoxicity of the higher doses of CS so that the calculated mutation frequencies, ie, the number of revertants per number of surviving bacteria, increased with doses up to 500 ug. This toxicity could be counteracted in part by the addition of increasing amounts of rat liver microsomes. In the view of these results, and taking into account the rare and low exposure of man, it is concluded that CS will not create a risk for the induction of point mutations or of carcinogenic processes mediated by DNA binding. (Author abstract) (26 Refs)

74 AU - Franc MC ; Maunier A ; Catilina P
AD - No affiliation given
TI - MUTAGENIC, TERATOGENIC OR TOXIC SUBSTANCES IN THE PREGNANT WOMAN WHICH MAY BE ENCOUNTERED IN THE WORKING ENVIRONMENT.
SI - ICDD/82/04568
SO - Arch Mal Prof Med Trav Secur Soc; 42(3):183-194 1981
LA - FRE
AB - Chemical and physical mutagenic and teratogenic agents and toxic substances to which pregnant women can be exposed in the working environment are reviewed. The occupational mutagens include benzene, benzo(a)pyrene, vinyl chloride and aflatoxins. Exposure of experimental animals to carcinogens during pregnancy caused increased tumor frequency in the first three generations. (196 Refs)

75 AU - Iosquin CJ
AD - Catedra de Medicina Interna A, Facultad de Ciencas Medicas, La Plata, Argentina
TI - PRIMARY HEPATIC CARCINOMA.
SI - ICDD/82/03752
SO - Rev Fac Cienc Plata; 4(2):27-31 1981
LA - SPA
AB - Primary hepatic carcinoma (PHC) was reviewed. The following

topics were discussed: etiology (cirrhosis, food, infections, parasites, hormones, thorotrast, As, and vinyl chloride), pathologic anatomy (tumors derived from the parenchyma or the mesenchyme), diagnosis (clinical, biological, and morphological), and treatment. (41 Refs)

76 AU - Mohrmann W
AD - Klinik fur Berufskrankheiten, Muncher Allee 10, D-8230 Bad Reichenhall, W. Germany
TI - ULTRASOUND DIAGNOSIS WITH EXAMPLES OF USE FROM OCCUPATIONAL MEDICINE.
SI - ICOB/82/03208
SO - Zentralbl Arbeitsmed Arbeitsschutz Proph; 31(10):398-401 1981
LA - GER
AB - Properties of ultrasound (US) and applications of US diagnosis in occupational medicine are described. US employs frequencies of 1-10 megahertz and detects acoustic differences in structure, such as between solid tissue and fluid. US is used in occupational medicine to detect conditions such as disease induced by vinyl chloride, and mesothelioma. (no Refs)

77 AU - Beaumont JJ ; Breslow NE
AD - Industrywide Studies Branch F-8, Natl. Inst. Occupational Safety and Health, 4676 Columbia Parkway, Cincinnati, OH, 45226
TI - POWER CONSIDERATIONS IN EPIDEMIOLOGIC STUDIES OF VINYL CHLORIDE WORKERS.
SI - ICOB/82/01134
SO - Am J Epidemiol; 114(5):725-734 1981
LA - ENG
AB - Nine retrospective mortality studies of workers exposed to vinyl chloride were reviewed to determine whether differences in their hypothesis testing results might be due to differences in statistical power. Where possible, the power of each study was calculated for cancer of the lung, brain and liver. When power was taken into consideration, the results for liver and brain cancer were found to be consistent with an etiologic role for vinyl chloride. For lung cancer, the data were not consistent with an etiologic role, in that two studies with very high power yielded negative results. (Author abstract) (16 Refs)

78 AU - Anderson D ; Richardson CR
AD - British Industrial Biological Res. Assoc., Woodmansterne Road, Carshalton, Surrey SM5 4DS, England
TI - ISSUES RELEVANT TO THE ASSESSMENT OF CHEMICALLY INDUCED CHROMOSOME DAMAGE IN VIVO AND THEIR RELATIONSHIP TO CHEMICAL MUTAGENESIS.
SI - ICOB/81/33319
SO - Mutat Res; 90(3):261-272 1981
LA - ENG
AB - Male Wistar rats were killed 6 or 24 hr after single or multiple exposure to clastogens, and bone marrow samples were prepared. Benzene, mitomycin C (MitC), ethyl methane sulfonate (EMS), trimethyl phosphate (TMP), and vinyl chloride (VC) constituted

the groups of clastogens analyzed. A statistically significant increase in percentage of abnormal cells above negative control values, as well as some increases in individual categories of chromosome damage were observed after treatment with each clastogen. Dose-response relationships were evident for benzene, EMS, and MitC. For TMP and VC only one dose level was tested. Gap incidence increased above that of other types of chromosome damage. Multiple exposure at the same sampling time and with the same route of administration produced similar or smaller total amounts of chromosome damage than single exposure. Higher yields of damage were obtained at 6 hr than at 24 hr after treatment with benzene. Benzene also produced a similar level of damage after ip injection or a single 2 hr exposure by inhalation. (13 Refs)

79 AU - Guengerich FP ; Geiger LE ; Hogy LL ; Wright PL
AD - Dept. Biochemistry and Center in Environmental Toxicology, Vanderbilt Univ. Sch. Medicine, Nashville, TN, 37232
TI - IN VITRO METABOLISM OF ACRYLONITRILE TO 2-CYANOETHYLENE OXIDE, REACTION WITH GLUTATHIONE, AND IRREVERSIBLE BINDING TO PROTEINS AND NUCLEIC ACIDS.
SI - ICDB/81/32562
SO - Cancer Res; 41(12):4925-4933 1981
LA - ENG
AB - The metabolism of the suspected carcinogen acrylonitrile was studied using subcellular fractions isolated from rats and humans. Irreversible binding of radioactive label from [1-14C]- or [2,3-14C]acrylonitrile to protein and DNA was enhanced by reduced nicotinamide adenine dinucleotide phosphate in the presence of rat liver microsomes or a reconstituted cytochrome P-450 system. During the reduced nicotinamide adenine dinucleotide phosphate-dependent reaction, HCN was produced, and the heme of cytochrome P-450 was destroyed. Rat brain microsomes did not produce detectable levels of metabolites. Conclusive evidence of metabolically mediated binding of acrylonitrile to protein and DNA in human systems was not found. With rats, metabolism was induced by pretreatment of animals with either phenobarbital or 5,6-benzoflavone. Labeled 2-cyanoethylene oxide was found to bind irreversibly to calf thymus DNA and microsomal protein. The extent of binding was greater in the case of 2,3-14C-labeled than 1-14C-labeled material. The relative first-order rate of acrylonitrile binding to calf thymus DNA in rat liver microsomal systems was one to two orders of magnitude less than that for 1,1,2-trichloroethylene and three orders of magnitude less than that for vinyl chloride or vinyl bromide. Rat liver microsomes or a reconstituted cytochrome P-450 system catalyzed the mixed-function oxidation of acrylonitrile to 2-cyanoethylene oxide. 2-Cyanoethylene oxide has a half-life of about 2 hr in neutral buffer at 37 C. This epoxide was found to serve as a substrate for microsomal epoxide hydrolase. HCN was released during hydrolysis of 2-cyanoethylene oxide or reaction of the epoxide with reduced glutathione; however, HCN release in either case was not stoichiometric with epoxide disappearance.

2-Cyanoethylene oxide reacted less rapidly with reduced glutathione than did acrylonitrile. Rat liver cytosol preparations contained glutathione S-transferase activity towards acrylonitrile and greater activity with 2-cyanoethylene oxide as a substrate. Cytosol preparations from rat brain and human liver had no detectable glutathione S-transferase activity towards acrylonitrile but did exhibit some activity towards 2-cyanoethylene oxide. These studies establish the basic pathways involved in the metabolism of acrylonitrile and should provide a basis for examination of the relevance of these individual steps and their roles in bioactivation and detoxication under more physiological situations. (Author abstract) (40 Refs)

80 AU - Theriault G ; Allard P
AD - Dept. Social and Preventive Medicine, Sch. Medicine, Laval Univ., Ste-Foy, Quebec, Canada
TI - CANCER MORTALITY OF A GROUP OF CANADIAN WORKERS EXPOSED TO VINYL CHLORIDE MONOMER.
SI - ICDB/81/31040
SO - JOM; 23(10):671-676 1981
LA - ENG
AB - The present study was undertaken to find out whether there was an excess of cancer mortality from causes other than angiosarcoma of the liver among a group of workers heavily exposed to vinyl chloride monomer (VCM). The mortality of 451 workers exposed to VCM for more than 5 yr was compared with that of 870 workers from the same company who had not been exposed to VCM. The relative risk for digestive cancer was significantly higher than 1 (6.25, confidence interval 2.69 to 14.52) in the exposed group. The standardized mortality ratio (SMR) for digestive cancer was also higher (SMR 259.26 p less than 0.01) than that of the general population. No other cancer was in excess. Since the exposed workers are known to have had a cigarette smoking experience similar to that of those who were not exposed, it is concluded that the association between lung cancer and VCM exposure, if present, is indeed rather small. (Author abstract) (25 Refs)

81 AU - Guengerich FP ; Mason PS ; Stott WT ; Fox TR ; Watanabe PG
AD - Dept. Biochemistry, Center Environmental Toxicology, Vanderbilt Univ. Sch. Medicine, Nashville, TN, 37232
TI - ROLES OF 2-HALOETHYLENE OXIDES AND 2-HALOACETALDEHYDES DERIVED FROM VINYL BROMIDE AND VINYL CHLORIDE IN IRREVERSIBLE BINDING TO PROTEIN AND DNA.
SI - ICDB/81/30770
SO - Cancer Res; 41(11,part1):4391-4398 1981
LA - ENG
AB - The metabolism of (1,2-14C)vinyl bromide (VBR) to products irreversibly bound to DNA and protein was examined in rat liver microsomes, reconstituted cytochrome P-450 systems, and isolated hepatocytes. A role for cytochrome P-450 was confirmed using inhibition and reconstitution experiments. The major form of cytochrome P-450 involved in VBR metabolism does not appear to be either of the major isozymes induced by phenobarbital or

beta-naphthoflavone, as determined by induction, reconstitution, and antibody inhibition studies. 2-Bromoethylene oxide and 2-bromoacetaldehyde, suspected metabolites of VBR, were synthesized and found to be substrates for rat liver epoxide hydrolase and equine liver alcohol dehydrogenase, respectively. These enzymes were used to probe the roles of the two possible metabolites in the irreversible binding of products of VBR to protein and DNA. Alcohol dehydrogenase was more effective than epoxide hydrolase in inhibiting the binding of VBR metabolites to protein in microsomal incubations. Epoxide hydrolase was effective in inhibiting the binding of VBR or vinyl chloride metabolites to calf thymus DNA added to such systems, but alcohol dehydrogenase was not. Similar results were obtained for binding of VBR metabolites to DNA in a reconstituted enzyme system. Reduced glutathione blocked nonenzymatic binding of 2-bromo(1,2-14C)acetaldehyde to protein but not DNA. Binding of vinyl chloride and VBR metabolites to protein was blocked by reduced glutathione, but binding to DNA was not. These results are consistent with the view that 2-haloethylene oxides are the major alkylating agents bound to DNA, and 2-haloacetaldehydes are the major alkylating agents bound to protein in these experimental systems. Studies with labeled 2-bromoacetaldehyde indicate that the slow kinetics of DNA binding by this compound is responsible in part for this phenomenon. Studies with isolated rat hepatocytes suggest that a significant portion of the total and reactive metabolites are able to leave these cells. In these systems, binding of metabolites of vinyl chloride to DNA outside the hepatocytes could be partially blocked by epoxide hydrolase or by alcohol dehydrogenase, implying that, as targets farther away from sources of reactive species are considered, the stabilities of these species become more important for reaction with nucleophilic sites. (Author abstract) (36 Refs)

82 AU - Konetzke GW
AD - Zentralinstitut fur Arbeitsmedizin der DDR, Noldnerstrasse 40-42, 1134 Berlin, E. Germany
TI - OCCUPATIONAL CANCER: PROBLEMS AND TASKS OF MEDICAL PRACTICE.
SI - ICDB/81/30709
SO - Z Aerztl Fortbild (Jena); 75(11/12):529-531 1981
LA - GER
AB - The problems of occupational cancer and its prevention are discussed. Aside from ionizing radiation, asbestos and chemical substances are the most important carcinogenic factors in the working environment. The number of industrial chemicals with demonstrated or probable carcinogenic effect is only 30-40. They include aminodiphenyl, arsenic, asbestos, auramines, benzene, benzidine, technical chloromethylmethylether, chromium, 2,2-dichlorodiethyl sulfide, dichlorodimethylether, beta-naphthylamine, nickel, tars, mineral oils, and vinyl chloride. Aflatoxins, acrylonitrile, beryllium, polychlorinated biphenyls, cadmium, dimethylcarbonylchloride, dimethylsulfate, ethyl oxide, and carbon tetrachloride are probable carcinogens. Occupational exposure to asbestos was definitely established in

303/743 patients with malignant mesothelioma, and occupational exposure was probable in 70. The prevention of occupational cancer includes the limitation of the use and production of carcinogenic substance to the extent absolutely necessary technologically, ban on especially hazardous carcinogens, compliance with occupational safety measures and hygienic standards, and check-up and monitoring of workers who have ever been exposed to carcinogenic factors. (7 Refs)

83 AU - Spit BJ ; Feron VJ ; Hendriksen CF
AD - Institute CIVO-Toxicology and Nutrition TNO, P.O. Box 360, 3700 AJ Zeist, The Netherlands
TI - ULTRASTRUCTURE OF HEPATIC ANGIOSARCOMA IN RATS INDUCED BY VINYL CHLORIDE.
SI - ICDB/81/29974
SO - Exp Mol Pathol; 35(2):277-284 1981
LA - ENG
AB - The hepatic angiosarcoma studied was from a male Wistar rat having been exposed to vinyl chloride monomer (VCM) by the oral route for 120 wk. Widened sinusoids lined by large electron-lucent, spindle-shaped tumor cells and membrane-bound nuclear-free structures were seen in the transitional zone between the tumor mass and the adjacent liver tissue. In areas merely consisting of tumor tissue the tumor cells had a more angular or irregular shape. The origin of the tumor cells is discussed in light of the characteristic differences between endothelial cells and Kupffer cells described in the literature. Although an endothelial origin of the tumor cells could not be established unequivocally, it was concluded that at present there is little reason to doubt such an origin. (Author abstract) (21 Refs)

84 AU - McDonald JC ; Harrington JM
AD - TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, London WC1E 7HT, England
TI - EARLY DETECTION OF OCCUPATIONAL HAZARDS.
SI - ICDB/81/29861
SO - J Soc Occup Med; 31(3):93-98 1981
LA - ENG
AB - Because of the rate of technological change, the time interval between exposure to a hazard and the appearance of its effects may be very long. Surveillance procedures for occupationally related diseases and injuries in Britain are generally regarded as inadequate. Reported intervals between the first suspicion and general acceptance of some occupational hazards have varied from 2 to 59 yr (for angiosarcoma due to vinyl chloride monomer and bladder cancer due to aromatic amines, respectively). Some occupational diseases have only been recognized by chance, having been completely missed by existing methods of reporting or the discovery was not reported. Detection of occupational hazards has frequently depended upon astute clinical observation; a system of rapid informal communication about such 'hunches' is needed. There are parallels for this idea in the history of determining

the etiology of numerous communicable diseases. The essentially informal reporting networks for communicable diseases operating in Britain and the United States are linked to central analysis units which can initiate rapid field studies when indicated. The establishment of an analogous system for occupational disease is advocated. (no Refs)

85 AU - Dabney BJ
AD - IBM Corporation, P.O. Box 1900, Boulder, CO, 80302
TI - THE ROLE OF HUMAN GENETIC MONITORING IN THE WORKPLACE.
SI - ICDB/81/27915
SO - JOM; 23(9):626-631 1981
LA - ENG
AB - The history and current state of some newer short-term tests for occupational genetic monitoring are reviewed. These are: cytogenetics, sister chromatid exchange, body fluid analysis, tests utilizing sperm, and detection of somatic cell variants. Occupational studies on benzene, vinyl chloride monomer, and epichlorohydrin are critically discussed from the standpoints of design and interpretation. It is concluded that these tests are not appropriate for risk assessment at the present time. Their clinical relevance, if any, is unknown. Proper validation and standardization have not been done, and design problems have often clouded the results of previous studies. There is a critical need for further research in the area of occupational genetic monitoring. Future applications should include integration with prospective morbidity and mortality studies, standardization of design and statistical methods, and development of new tests with genetically relevant endpoints. (Author abstract) (44 Refs)

86 AU - Rodnan GP
AD - Div. Rheumatology and Clinical Immunology, Dept. Medicine, Univ. Pittsburgh, Pittsburgh, PA, 15261
TI - WHEN IS SCLERODERMA NOT SCLERODERMA? THE DIFFERENTIAL DIAGNOSIS OF PROGRESSIVE SYSTEMIC SCLEROSIS.
SI - ICDB/81/27247
SO - Bull Rheum Dis; 31(2):7-10 1981
LA - ENG
AB - Cutaneous plaques or nodules resembling those of progressive systemic sclerosis (PSS; systemic scleroderma) may develop in workers exposed to vinyl chloride or trichloroethylene. Chemotherapy which bleomycin often causes PSS-like fibrosis, which subsides when the agent is discontinued. Several disorders, including the carcinoid syndrome and myeloma-associated amyloidosis, may be characterized by PSS-like skin thickening. Differential diagnosis is usually not difficult, because the visceral components of PSS are absent and/or the characteristic clinical features of the underlying disease are present. (20 Refs)

87 AU - Selikoff IJ
AD - Environmental Science Lab., Dept. Community Medicine, Mount Sinai Sch. Medicine, City Univ. New York, New York, NY, 10029
TI - CARCINOGENIC RISK MANAGEMENT IN THE UNITED STATES.
SI - ICDB/81/26715
SO - Ann NY Acad Sci; 363:283-293 1981
LA - ENG
AB - Carcinogenic risk management is in the developmental stage in the United States. Data from studies of smoking, asbestos, and vinyl chloride have shown the effect of carcinogen dose on the incidence and development of cancers. As a result, the yes-or-no approach to carcinogens has been replaced by regulation based on the dose-response approach. Observation and regulation of carcinogens is being extended from the workers who produce them to include anyone who is exposed during the life of the carcinogens. Other aspects under study include latency, absence of thresholds, dose-induction periods, and multiple factor interactions. The extrapolation of animal data to man remains a debated subject. Observations indicate that, with at least some carcinogens, risk is reduced in time if exposure to the carcinogen ceases. The relationship between mutagenicity and carcinogenicity is still uncertain. The reproductive effects of carcinogens and the decision to ban or control them present ethical and legal questions that remain unanswered. (15 Refs)

88 AU - Preuss PW
AD - Health Sciences, United States Consumer Product Safety Commission, Washington, DC
TI - THE ELIMINATION OF CARCINOGENIC RISKS IN CONSUMER PRODUCTS.
SI - ICDB/81/26704
SO - Ann NY Acad Sci; 363:63-78 1981
LA - ENG
AB - Statutes of the Consumer Product Safety Commission (CPSC) designed to assure that marketed products do not cause injury or illness are reviewed. Regulatory techniques include dissemination of product information to the media and consumers, labeling of consumer products, establishing performance or other standards, and banning certain consumer products. On six occasions in its 8 yr of existence, the CPSC has determined that the products contain materials which present a risk of human cancer. Each of the six regulatory actions were unique. The products involved included vinyl chloride, asbestos tris(hydroxymethyl)aminomethane (TRIS), and benzene. Problems associated with balancing the risks, costs, and benefits are reviewed. An appendix containing the CPSC proposed methodology for commission consideration of findings under section 9(c) of the Consumer Product Safety is included. (no Refs)

89 AU - Anderson D ; Richardson CR ; Purchase IF ; Evans HJ ; O'Riordan ML
AD - Central Toxicology Lab., Imperial Chemical Industries, Ltd., Alderley Park, Macclesfield, Cheshire SK10 4TJ, England
TI - CHROMOSOMAL ANALYSIS IN VINYL CHLORIDE EXPOSED WORKERS: COMPARISON OF THE STANDARD TECHNIQUE WITH THE SISTER-CHROMATID EXCHANGE TECHNIQUE.
SI - ICDB/81/26470
SO - Mutat Res; 83(1):137-144 1981
LA - ENG
AB - Twenty-one workers exposed to vinyl chloride (VC) and six controls were subjected to conventional chromosomal analysis (CA) and the determination of sister-chromatid exchanges (SCE). In addition, SCE in human lymphocytes were studied before and after exposure to gaseous VC in vitro. These workers had been subjected to studies 18 mo before. In the exposed workers the av of the different types of abnormalities were significantly increased with CA, while only a slight, nonsignificant, increase of SCE was noted in the exposed group compared with the controls. In lymphocyte cultures exposed to VC during G0/early G1, and late G1/early S phase, no increase in SCE was noted without metabolic activation; a marked decrease was noted with activation and this was independent of cell cycle phase. The small increases of SCE in workers were attributed to low exposures rather than the inability of VC to induce SCE in human lymphocytes; the SCE levels could have returned to normal relatively quickly after exposure. It is suggested that SCE analysis might not be of much value after very low chronic chemical exposures, but might be useful during high chronic chemical exposures and during the first few days after acute exposure. (19 Refs)

90 AU - Vianna NJ ; Brady JA ; Cardamone AT
AD - Bureau Environmental Epidemiology and Occupational Health, Albany, New York State Dept. Health, NY
TI - EPIDEMIOLOGY OF ANGIOSARCOMA OF LIVER IN NEW YORK STATE.
SI - ICDB/81/25590
SO - NY State J Med; 81(6):895-899 1981
LA - ENG
AB - The geographic distribution of angiosarcoma of the liver (ASL) among residents of New York was examined with special emphasis on the epidemiologic characteristics which might be of etiologic importance in this malignancy. The av annual incidence rate for the state, excluding New York City, was 0.26 per million population. Of the chemicals associated with ASL, potential exposure to vinyl chloride appeared to be the most important factor in certain urban industrialized counties, whereas probable arsenic exposure was the major factor in rural areas. Prior thorium dioxide injections accounted for only 7% of the 43 patients studied. We suggest that certain chemicals structurally similar to vinyl chloride might be of etiologic importance among patients who have no documented exposure to any of the established causes of ASL. (Author abstract) (25 Refs)

91 AU - Duverger M ; Lambotte M ; Malvoisin ; De Meester C ; Poncelet F
AU - Mercier M
AD - (c/o Poncelet) Lab. Biotoxicology, Univ. Louvain Sch. Pharmacy, U.C.L.-73.69, B. 1200 Brussels, Belgium
TI - METABOLIC ACTIVATION AND MUTAGENICITY OF 4 VINYLIC MONOMERS (VINYL CHLORIDE, STYRENE, ACRYLONITRILE, BUTADIENE).
SI - ICDB/81/25504
SO - Toxicol Eur Res; 3(3):131-140 1981
LA - ENG
AB - Literature data on the mutagenic activity and metabolism of monomers vinyl chloride (VCM), styrene (STY), acrylonitrile (ACN) and butadiene (BUT) are reviewed. Vinylic monomers were shown to be susceptible to metabolic conversion by the mixed function oxidase of the endoplasmic reticulum into primary reactive intermediates (oxiranes). VCM, STY, ACN, and BUT were mutagenic in Salmonella typhimurium test system. VCM was shown to induce recessive lethals in Drosophila melanogaster. Incubation of Chinese hamster cells with VCM produced a dose-dependent mutagenicity and cytotoxicity. An increased frequency of chromosome aberrations was recorded in workers who had an occupational exposure to VCM and STY. (130 Refs)

92 AU - Hong CB ; Winston JM ; Thornburg LP ; Lee CC ; Woods JS
AD - (c/o Woods) Battelle Seattle Res. Center, 4000 N.E. 41st St., Seattle, WA, 98105
TI - FOLLOW-UP STUDY ON THE CARCINOGENICITY OF VINYL CHLORIDE AND VINYLIDENE CHLORIDE IN RATS AND MICE: TUMOR INCIDENCE AND MORTALITY SUBSEQUENT TO EXPOSURE.
SI - ICDB/81/25472
SO - J Toxicol Environ Health; 7(6):909-924 1981
LA - ENG
AB - The development and incidence of neoplastic changes and other effects during a 12-mo exposure follow-up period in male and female albino CD-1 mice and CD rats exposed to vinyl chloride (VC) or vinylidene chloride (VDC) for various lengths of time were evaluated. Eight to 28 mice of each sex and 4-16 rats of each sex were exposed to 50, 250, or 1,000 ppm VC, 55 ppm VDC, or filtered air for 6 hr/day, 5 days/wk. Exposure of mice and rats to VC for 1, 3, and 6 mo and 1, 3, 6, and 10 mo, respectively, increased the number of deaths and increased moribundity at all dose levels during the exposure and postexposure periods. The cumulative tumor incidence for essentially all organ sites in animals exposed to 50 ppm VC or 55 ppm VDC was similar to that in controls (except for mammary gland tumors in female mice). Only at higher dose levels of VC did significant increases in cumulative tumor incidence occur. Cumulative tumor incidence during the period after VC exposure increased with duration of exposure, independent of dose level. The implication of the findings with respect to the assessment of cancer risk resulting from exposure of humans to VC and perhaps other carcinogens is discussed. (23 Refs)

93 AU - Feron VJ ; Hendriksen CF ; Speek AJ ; Til HP ; Spit BJ
AD - Inst. CIVO - Toxicology and Nutrition TNO, PO Box 360, 3700 AJ, Zeist, The Netherlands
TI - LIFESPAN ORAL TOXICITY STUDY OF VINYL CHLORIDE IN RATS.
SI - ICDB/81/23949
SO - Food Cosmet Toxicol; 19(3):317-333 1981
LA - ENG
AB - Vinyl chloride monomer (VCM) was administered to five groups each of 60-80 male or 60-80 female Wistar rats by incorporating polyvinyl chloride (PVC) containing the VCM into the diet or by gastric intubation of 10% VCM soln in soya-bean oil. The actual exposures to the VCM provided by the PVC were 0 (control), 1.7, 5.0, and 14.1 mg/kg body wt/day, and that provided by the VCM soln was 300 mg/kg body wt/day for 5 days/wk. Following the administration of the VCM, the rats were studied with respect to behavior and appearance, body wt and food consumption, mortality, gross liver pathology, light microscopy of the liver and other organs, and electron microscopy of the hepatic parenchyma. The study indicated that the incorporation of VCM-containing PVC powder into the diets of rats is an effective method for studying the long-term effects of oral administration of the VCM. When administered to the rats, the tumor response of the rat liver seemed to shift from an almost exclusive development of angiosarcomas at very high levels of exposure to the exclusive induction of hepatocellular tumors at low levels of exposure. There were also some evidence the ingestion of VCM in PVC enhanced the development of abdominal mesotheliomas and of mammary adenocarcinomas. (61 Refs)

94 AU - Eckardt F ; Muliawan H ; De Ruiter N ; Kappus N
AD - Institut fur Biologie, Gesellschaft fur Strahlen- und Umweltforschung, Ingolstadter Landstr. 1, D-8042 Neuherberg, W. Germany
TI - RAT HEPATIC VINYL CHLORIDE METABOLITES INDUCE GENE CONVERSION IN THE YEAST STRAIN D7RAD IN VITRO AND IN VIVO.
SI - ICDB/81/22237
SO - Mutat Res; 91(4/5):381-390 1981
LA - ENG
AB - D7RAD, an indicator strain of the yeast Saccharomyces cerevisiae, was injected iv into male Wistar rats which were then exposed to vinyl chloride (VC) gas. After 24 hr of VC inhalation, the number of gene convertants scored as tryptophan prototrophic colonies in the yeast cells harvested from the livers of test animals were significantly increased compared with those of untreated controls. A model for VC tumorigenesis is described. (40 Refs)

95 AU - Ballin JS
AD - Control Action Div., Office Toxic Substances, United States Environmental Protection Agency, Washington, DC
TI - DON'T TAKE YOUR 'WORK' HOME WITH YOU.
SI - ICDB/81/21751
SO - Occup Health Saf; 50(6):39-42 1981
LA - ENG
AB - The recognition that occupational exposure to toxic chemicals can affect the worker and his or her family is a new concept in work-related disease. Various routes of family exposure are illustrated with respect to worker exposure to anesthetic gases, lead, vinyl chloride, dioxin, polychlorinated biphenyls, methylmercury, diethylstilbestrol, ionizing radiation, asbestos, beryllium, Kepone, and others. Data concerning beryllium and asbestos exposure are discussed in detail. (20 Refs)

96 AU - Fortwengler HP ; Jones D ; Espinosa E ; Tamburro CH
AD - (c/o Tamburro) Div. Digestive Diseases and Nutrition, Dept. Medicine, Health Sciences and Cancer Center, Univ. Louisville, Louisville, KY, 40292
TI - EVIDENCE FOR ENDOTHELIAL CELL ORIGIN OF VINYL CHLORIDE-INDUCED HEPATIC ANGIOSARCOMA.
SI - ICDB/81/19359
SO - Gastroenterology; 80(6):1415-1419 1981
LA - ENG
AB - Previous reports of hepatic angiosarcoma have not clearly defined the cellular type from which this tumor arises, as evidenced by the terminology of endothelioma, Kupffer cell sarcoma, endothelial cell sarcoma, and hemangioendothelial sarcoma, etc, which have been used interchangeably. In addition, there has been no consensus on the separate entity of Kupffer and sinusoidal endothelial cells. In the work presented here, evidence for the endothelial cell origin of this tumor is provided by the demonstration of factor VIII, a known endothelial cell marker, in the tumor cells. Fluorescence due to the presence of factor VIII appeared intense in the tumor sinusoidal cells of all four vinyl chloride-associated angiosarcomas studied, whereas normal liver sinusoidal lining cells showed negligible fluorescence. (Author abstract) (25 Refs)

97 AU - Wisniewska-Knypl JM ; Sokal JA ; Klimczak J ; Dajniak A
AU - Bogdanikowa B
AD - Industrial Toxicology Branch, Inst. Occupational Medicine, Teresy 8, 90-950 Lodz, Poland
TI - PROTECTIVE EFFECT OF METHIONINE AGAINST VINYL CHLORIDE-MEDIATED DEPRESSION OF NON-PROTEIN SULPHYDRYLS AND CYTOCHROME P-450.
SI - ICDB/81/19108
SO - Toxicol Lett; 8(3):147-152 1981
LA - ENG
AB - The protective effect of DL-methionine (MET: 1 g/kg by gavage) against vinyl chloride (VC)-mediated hepatotoxicity was assessed in rats induced by phenobarbital (PB) and exposed to 50,000 ppm

VC for 5 hr. The MET prevented the enormous liver hypertrophy, non-protein -SH depletion, destruction of P-450, and inhibition of microsomal protein synthesis, which were seen after VC exposure without MET. The use of MET as a prophylactic agent in cases of occupational exposure to VC was suggested. (20 Refs)

98 AU - Kurliandskii BA ; Stovbur NN ; Turusov VS
AD - Municipal Sanitary Epidemiologic Station, Moscow, USSR
TI - SANITARY REGULATIONS OF VINYL CHLORIDE.
SI - ICDB/81/17468
SO - Gig Sanit; (3):74-75 1981
LA - RUS
AB - Albino rats were treated with various doses of vinyl chloride (VC) to evaluate the general toxicity and carcinogenic effect of this substance so that its max permissible concentration (MPC) in the air of the working zone could be determined. The VC concentration of 5 mg/cubic meter is considered to be close to the threshold level in terms of general toxicity. A correlation was found between the development of tumors (including VC-specific angiosarcomas) and the VC dose. The results were considered to indicate that VC belongs to carcinogens of low activity (class IV of blastomogenic activity). It was recommended that the VC concentration of 0.1 mg/cubic meter be regarded as a MPC in the air of the working zone. (15 Refs)

99 AU - Koischwitz D ; Lelbach WK ; Lackner K ; Hermanutz D
AD - Rontgenabteilung Medizinische Klinik, Radiologische Klinik der Universitat Bonn, 5300 Bonn-Venusberg, W. Germany
TI - VINYL CHLORIDE-INDUCED ANGIOSARCOMA AND HEPATOCELLULAR CARCINOMA OF THE LIVER.
SI - ICDB/81/17109
SO - Roefo: Fortschritte Auf Dem Gebiete Der Roentgenstralen Und Der; 134(3):283-290 1981
LA - GER
AB - Presentation, diagnosis, and course of hepatic malignancies associated with exposure to vinyl chloride (VC) are illustrated through the case histories of three patients (54-57-yr-old men). The duration of known exposure to VC for these patients was 9-21 yr. Common signs at initial presentation included hepatomegaly, thrombocytopenia, splenomegaly, and history of diabetes mellitus. Two of the patients had elevated levels of alkaline phosphatase. Initial radiologic and histologic examinations revealed cirrhosis, siderosis, and/or fibrosis of the liver in all three patients. All of the patients developed esophageal varices in the course of the disease. The interval between initial presentation and diagnosis of hepatic tumors ranged from 1 to 11 yr; the presence of malignancies was confirmed through the use of celiacography, sonography, selective hepaticography, indirect splenoportography, and computer tomography. One patient developed osteolytic metastases and one developed multiple brain metastases. The conditions of the patients deteriorated rapidly after the final diagnoses were made, and each of the patients died within a few mo of the final diagnosis. Autopsies revealed

that the patients had hemangiosarcoma of the right hepatic lobe, multicentric angiosarcoma combined with multicentric primary hepatocellular carcinoma, or metastatic angiosarcoma of the liver. Spontaneous occurrence of angiosarcomas, irregular presentation of such tumors, and the relationship of the development of these tumors to VC exposure are discussed. (52 Refs)

100 AU - Hallstrom I ; Sundvall A ; Rannug U ; Grafstrom R ; Ramel C
AD - Environmental Toxicology Unit, Wallenberg Lab., Univ. Stockholm, S-106 91 Stockholm, Sweden
TI - THE METABOLISM OF DRUGS AND CARCINOGENS IN ISOLATED SUBCELLULAR FRACTIONS OF DROSOPHILA MELANOGASTER. I. ACTIVATION OF VINYL CHLORIDE, 2-AMINOANTHRACENE AND BENZO(A)PYRENE AS MEASURED BY MUTAGENIC EFFECTS IN SALMONELLA TYPHIMURIUM.
SI - ICDB/81/13499
SO - Chem Biol Interact; 34(2):129-143 1981
LA - ENG
AB - The capacity of microsomal fractions from different Drosophila strains to activate three premutagens, 2-aminoanthracene (2-AA) vinyl chloride (VCM) and benzo(a)pyrene (BP) was investigated, using Salmonella typhimurium as the indicator organism. A significant increase in the mutation response in the Salmonella test system was obtained with all three substances in the presence of a metabolizing system (S9) from Drosophila larvae. 2-AA was converted to highly mutagenic metabolite(s) by the Drosophila S9 and the mutagenic effect was further increased after pretreatment with Aroclor 1254 (PCB) or beta-naphthoflavone (BNF). BP has only marginal mutagenic effects, causing less than a 2-fold increase in the number of mutants over the control. The data indicate that the metabolic conversion of BP is different in the Drosophila as compared to the rat liver microsomal fraction. In accordance with mutagenic data on Drosophila in vivo, vinyl chloride was a fairly weak mutagen in this Drosophila-Salmonella in vitro system. (Author abstract) (42 Refs)

101 AU - Stott WT ; Watanabe PG
AD - Toxicology Res. Lab., Dow Chemical, 1803 Building, Midland, MI, 48640
TI - RISK ASSESSMENT OF EXPOSURE TO VINYL CHLORIDE.
SI - ICDB/81/12697
SO - Pure Appl Chem; 53(2):593-595 1981
LA - ENG
AB - Carcinogenic risk estimation of human exposure to vinyl chloride (VC) was determined by utilizing laboratory animal data on the chronic bioassay of VC, VC pharmacokinetics and VC macromolecular interaction. The impact of these data upon the type of risk VC may pose to humans and the selection of appropriate mathematical models to quantitatively estimate 'risk' are discussed. (Author abstract) (6 Refs)

102 AU - Heckman JH
AD - Washington, DC, 20036
TI - REGULATORY STATUS OF POLYVINYL CHLORIDE, 1980.
SI - ICDB/81/12696
SO - Pure Appl Chem; 53(2):583-592 1981
LA - ENG
AB - The regulatory history of vinyl chloride and polyvinyl chloride, particularly at the Occupational Safety and Health Administration, the Food and Drug Administration, and the Environmental Protection Agency, is reviewed in detail. It is evaluated in terms of perceptions of the soundness of governmental actions and also as an example of responsible industry achievement. Despite constant reevaluation by the involved agencies, the urgency that initially characterized their actions regarding vinyl chloride has been tempered by continuing improvements in monomer management and recently maturing concepts of risk assessment. The most valuable benefit to flow from the vinyl chloride experience may well be its influence in focusing attention on the need for more objective risk assessment as an accepted basis for all regulatory decision-making. (Author abstract) (27 Refs)

103 AU - Dannaher CL ; Tamburro CH ; Yam LT
AD - Columbus Hosp. Regional Oncology Center, Post Office Box 5013, Great Falls, MT, 59403
TI - OCCUPATIONAL CARCINOGENESIS: THE LOUISVILLE EXPERIENCE WITH VINYL CHLORIDE-ASSOCIATED HEPATIC ANGIOSARCOMA.
SI - ICDB/81/11778
SO - Am J Med; 70(2):279-287 1981
LA - ENG
AB - Hepatic angiosarcoma in man was first associated with exposure to vinyl chloride in Louisville, Kentucky, where it was identified in 10 persons from a single vinyl chloride polymerization plant; clinical manifestations are summarized herein. Following prolonged exposure to vinyl chloride, the onset of this disease is insidious and the clinical picture is that of nonspecific hepatic injury with mildly abnormal biochemical liver test results. Carcinoembryonic antigen and alpha fetoprotein are undetectable. Radionuclide and angiographic studies of liver show characteristic but nondiagnostic abnormalities. A definite diagnosis is usually made only by open liver biopsy. Treatment is unsatisfactory but chemotherapy seems to prolong survival. Av survival from diagnosis is about 12 mo. Overt liver failure usually occurs only as a preterminal event and was the major cause of death in all of our patients. Preventive measures are now in effect in the plant. This experience illustrates the importance of the clinician in occupationally-related cancer. (Author abstract) (58 Refs)

104 AU - Popper H ; Selikoff IJ
AD - Stratton Lab. Study Liver Diseases, Environmental Sciences Lab., Mount Sinai Sch. Medicine, City Univ. New York, One Gustave Levy Place, New York, NY, 10029
TI - WHAT IS ENVIRONMENTAL PATHOLOGY?
SI - ICDB/81/11378
SO - Am J Med; 70(2):218-220 1981
LA - ENG
AB - Environmental hazards that effect man have been of growing concern. Data concerning these hazards is accumulating. This information comprises the field of environmental pathology. The liver serves as a study model for many environmental injuries since it is the principal target of many hazardous environmental agents. However, hepatocellular carcinoma, with the exception of aflatoxicosis and vinyl chloride, is not often the result of environmental carcinogens. Continued vigilance is encouraged since other agents may yet be detected that resemble vinyl chloride. Two proposed restrictions of the definition of environmental pathology reflect the dose and duration of exposure and the source of exposure. These restrictions lessen unjustified concerns and focus on potentially greater hazards. (12 Refs)

105 AU - Spengler S ; Singer B
AD - Dept. Molecular Biology and Virus Lab., Univ. California Berkeley, Berkeley, CA, 94720
TI - TRANSCRIPTIONAL ERRORS AND AMBIGUITY RESULTING FROM THE PRESENCE OF 1,N6-ETHENOADENOSINE OR 3,N4-ETHENOCYTIDINE IN POLYRIBONUCLEOTIDES.
SI - ICDB/81/10893
SO - Nucleic Acids Res; 9(2):365-373 1981
LA - ENG
AB - The compounds 1,N6-ethenoadenosine (epsilonA) and 3,N4-ethenocytidine (epsilonC) in copolymers with unmodified nucleosides were transcribed using DNA-dependent RNA polymerase in the presence of Mn++. Nearest neighbor analysis of the products showed that epsilonA directed incorporation of A greater than U greater than C while epsilonC directed the incorporation of U greater than or equal to A much greater than C. Neither directed G into the complementary polymer. Such misincorporations resulting from epsilonA and epsilonC, compounds that are formed in vivo by the carcinogen vinyl chloride, may have a biological role as promutagens. (Author abstract) (28 Refs)

106 AU - Barbin A ; Bartsch H ; Leconte P ; Radman M
AD - Div. Environmental Carcinogenesis, International Agency Res. Cancer, 150 cours Albert-Thomas, F-69372 Lyon Cedex 2, France
TI - STUDIES ON THE MISCODING PROPERTIES OF 1,N6-ETHENOADENINE AND 3,N4-ETHENOCYTOSINE, DNA REACTION PRODUCTS OF VINYL CHLORIDE METABOLITES, DURING IN VITRO DNA SYNTHESIS.
SI - ICDB/81/10892
SO - Nucleic Acids Res; 9(2):375-387 1981
LA - ENG

AB - The compounds 1,N6-ethenoadenine (epsilonA) and 3,N4-ethenocytosine (epsilonC) are formed when electrophilic vinyl chloride (VC) metabolites, chloroethylene oxide (CEO) or chloroacetaldehyde (CAA) react with adenine and cytosine residues in DNA. They were assayed for their miscoding properties in an in vitro system using Escherichia coli DNA polymerase I and synthetic templates prepared by reaction of poly(dA) and poly(dC) with increasing concentrations of CEO or CAA. Following the introduction of etheno groups, an increasing inhibition of DNA synthesis was observed. dGMP was misincorporated on CAA- or CEO-treated poly(dA) templates and dTMP was misincorporated on CAA- or CEO-treated poly(dC) templates, suggesting that epsilonA and epsilonC may miscode. The error rates augmented with the extent of reaction of CEO or CAA with the templates. Base-pairing models are proposed for the epsilonA-G and epsilonC-T pairs. The potentially miscoding properties of epsilonA and epsilonC may explain why metabolically-activated VC and its reactive metabolites specifically induce base-pair substitution mutations in Salmonella typhimurium. Promutagenic lesions may represent one of the initial steps in VC- or CEO-induced carcinogenesis. (Author abstract) (58 Refs)

107 AU - Dannaher CL ; Tamburro CH ; Yam LT
AD - Regional Oncology Center, Columbus Hosp., P. O. Box 5013, Great Falls, MT, 59403
TI - CHEMOTHERAPY OF VINYL CHLORIDE-ASSOCIATED HEPATIC ANGIOSARCOMA.
SI - ICDB/81/09500
SO - Cancer; 47(3):466-469 1981
LA - ENG
AB - The use of systemic chemotherapy was studied in a group of four patients who had hepatic angiosarcoma in association with exposure to vinyl chloride. All of the patients received adriamycin 60 mg/square meter (m2) iv every 3-4 wk and in three patients this was combined with Cytoxan 600 mg/m2 and methotrexate 20 mg/m2. Three patients had an objective response lasting 4, 9, and 10 mo. One patient had stable disease for 10 mo. Responding patients maintained an excellent performance status during therapy. Following evidence of progressive disease, patients died in 3, 4, and 6 mo. Survival from the time of diagnosis was 11, 13, 15 and 53+ mo. Sufficient data are not available from these patients to recommend a specific drug or combination for use in hepatic angiosarcoma, but our data indicate that chemotherapy can improve quality and duration of survival. (Author abstract) (12 Refs)

108 AU - Spengler SJ ; Singer BA
AD - University of California, Berkeley, CA, 94720
TI - 1,N(6)-ETHENOADENOSINE AND 3,N(4)-ETHENOCYTIDINE IN POLYRIBONUCLEOTIDES LEAD TO TRANSCRIPTIONAL ERRORS AND AMBIGUITY (MEETING ABSTRACT).
SI - HERN/82/09774
SO - J Supramol Struct; Suppl5:212 1981
LA - ENG

AB - The human carcinogen, vinyl chloride, is metabolically converted by the microsomal cytochrome P-450-dependent monooxygenases to the reactive compound chloroethylene oxide, which also rearranges to form chloroacetaldehyde. These compounds react with adenosine and cytidine to form the fluorescent etheno derivatives, 1,N(6)-ethenoadenosine (epsilonA) and 3,N(4)-ethenocytidine (epsilon C). We have synthesized C and A ribopolymers containing varying amounts of epsilon C or epsilon A and transcribed them using DNA-dependent RNA polymerase in the presence of Mn. Nearest neighbor analysis of the transcripts showed that epsilon A acted more like U than like A and more like A than G. Etheno C, on the other hand, acts primarily like A, though simulation of U and G also occurred. Neither derivative behaved like C in these copolymers. Such transcriptional errors may indicate the nature of the mutagenic lesion involved in vinyl chloride carcinogenesis, since it has been shown that even at low doses these derivatives accumulate in DNA. (1 Ref)

109 AU - Hall JA ; Saffhill R

AD - Paterson Laboratories, Christie Hospital & Holt Radium Institute, Manchester M20 9BX

TI - CHLOROACETALDEHYDE, A VINYL CHLORIDE METABOLITE, INDUCES ERRORS DURING IN VITRO DNA SYNTHESIS (MEETING ABSTRACT).

SI - HERN/82/07208

SO - 22nd Annual General Meeting of the British Association for Cancer Research, April 13-15, 1981, Keele, Staffordshire, England. The Association 87 pp., 1981.

LA - ENG

AB - Chloroacetaldehyde (CA), a rearranged metabolic product of the human carcinogen vinyl chloride has been shown to be mutagenic in certain microbial systems as well as towards mammalian cells. CA has been reacted with the alternating DNA-like polymers poly(deoxyadenylate-thymidylate)(poly(dA-dT)) and poly(deoxycytidylate-guanylate)(poly(dC-dG)) when, as with DNA etheno-adducts of the adenine and cytosine bases are formed. These treated polymers, when used as templates for E coli DNA polymerase I, show a decreased ability to direct DNA synthesis. This is accompanied by an increase in the relative levels of non-complementary nucleotides incorporated into the newly synthesized DNA-like material. This increased with the amount of modified base present in the templates used. With the poly(dA-dT) templates one deoxythymidine monophosphate residue was incorporated for every approx 60 ethenoadenine residues present while no deoxycytidine monophosphate misincorporation was detected. One misincorporation of deoxy AMP or deoxythymidine monophosphate occurred in the presence of approx 30 and 60 ethenocytosine residues respectively in the poly(dC-dG) templates. For the modified poly (dC-dG) templates a nearest neighbor analysis shows that the majority of the errors were incorporated opposite the cytosine (or modified cytosine) bases. Extensive analyses of the modifications present in the templates indicate that the misincorporations observed are not due to the presence of apurinic sites or to the formation of uracil or

xanthine by deamination of the the cytosine or adenine bases respectively. We conclude that the non-complementary nucleotide incorporations probably arise from the presence of etheno-adducts in the templates used. (no Refs)

110 AU - Rice J ; Frith C
AD - Laboratory of Experimental Pathology, National Cancer Institute, Bethesda, MD
TI - CRITERIA FOR ESTABLISHING ORGAN SPECIFICITY IN EXPERIMENTAL CHEMICAL CARCINOGENESIS (MEETING ABSTRACT).
SI - HERN/82/05944
SO - Organ and Species Specificity in Chemical Carcinogenesis Symposium, March 2-4, 1981, Raleigh, North Carolina. U.S. Environmental Protection Agency 96 pp., 1981.
LA - ENG
AB - Chemical carcinogens often have different effects in different species; a given agent causes neoplasms in different organs and tissues depending on the species, sex, and age of the recipient and on the magnitude, schedule, and route of exposure. Such differences can provide a means of experimentally distinguishing interactions of carcinogen with target cells that are significant for carcinogenesis. A given agent may affect different organ systems in different species: aromatic amines, for example, are preferentially carcinogenic for the urinary bladder in man, non-human primates, and the Syrian hamster, but are more likely to affect the liver or intestinal mucosa, or even remote organs such as Zymbal's gland in the rat, and are totally ineffective in other species that lack the metabolic capacity to N-hydroxylate and conjugate these compounds. Alternatively, a given agent may affect the same organ system in different species, but the target cell may vary. Diethylnitrosamine (DEN) is carcinogenic for hepatocytes in most species, including the mouse, rat, Syrian hamster, and dog, but in some species, including the mouse, rat, and dog, DEN is also carcinogenic for the hepatic blood vessels. Conversely, vinyl chloride is preferentially carcinogenic for the blood vessels of the liver in man and in rats and mice, in which species both vascular and epithelial tumors may also be induced at extrahepatic sites. As an indication of the importance of systematic pathological evaluation in such studies, a comparison of gross and microscopic evaluation of tissues from mice given 2-acetylaminofluorene is presented. (no Refs)

111 AU - Natch GG ; Mamay PD ; Christenson CC ; Casto BC ; Langenbach R
AU - Nesnow S
AD - Northrop Services, Inc, Research Triangle Park, NC
TI - IN VITRO TRANSFORMATION OF HAMSTER EMBRYO CELLS EXPOSED TO GASEOUS OR VOLATILE CHLORINATED HYDROCARBONS (MEETING ABSTRACT).
SI - HERN/82/05251
SO - Proc Am Assoc Cancer Res; 22:119 1981
LA - ENG
AB - Chlorinated organic compounds, many of which are volatile liquids or gases have widespread industrial and environmental importance and have a suspected role in the etiology of certain human

cancers. Methods have been developed in our laboratory for exposing cultured cells to gases or vapors of volatilized liquids. These techniques allow the evaluation of the genotoxic effects of these agents in in vitro systems. Primary hamster embryo cells were treated with acetone (negative control) or varying concentrations of the following chlorinated hydrocarbons: 1,1,1 trichloroethane, (TCE); dichloromethane (DCM): 1,1-dichloroethane (DCE1); 1,2 dichloroethane (DCE2) or vinyl chloride (VC), and subsequently assayed for cell survival and an increased sensitivity to SA7 virus transformation. Treatment doses extended from toxic to several nontoxic doses. Samples from each test chamber were analyzed by standard gas chromatographic techniques and actual concentrations determined. TCE, DCM, DCE1, DCE2, and VC treated cells demonstrated an increased frequency of transformation by SA7 virus. Treatment chamber concentrations of chemicals producing a maximal response ranged from approx 11-26 ug/cm3 (TCE), 22-72 ug/cm3 (DCM), 14-73 ug/cm3 (DEC2) and 194 ug/cm3 (VC). The length of chemical treatment and the time interval before subsequent addition of transforming virus was critical and dependent on the chemical evaluated. Incorporation of these compounds into liquid cell culture medium were unsuccessful or produced only a weak enhancement response. Treatment of hamster cells with gases or the vapor phase of volatile compounds yielded reproducible and quantitative results. (no Refs)

112 AU - Kucerova M
AD - Genetic Department, Postgraduate Medical Institute, Prague, Czechoslovakia
TI - COMPARISON OF DIFFERENT CHROMOSOMAL DAMAGE CAUSED IN VIVO IN HUMAN CELLS BY DIFFERENT CHEMICAL MUTAGENS (MEETING ABSTRACT).
SI - HERN/81/02903
SO - Eleventh Annual Meeting of the European Environmental Mutagen Society, July 6-11, 1981, Budapest, Hungary The Society, 1981.
LA - ENG
AB - Summarizing for cytogenetic studies of people exposed in vivo to different mutagens (epichlorhydrine, vinyl chloride, imuran and cyclophosphamide) we compare the resulting chromosomal damage, which was very similar. However, the chromosomal aberrations in human lymphocytes detected after exposure to chemicals in vivo on whole differ enormously from chromosomal aberrations discovered in human lymphocytes after exposure to radiation in vivo. (no Refs)

113 AU - Sram RJ
AD - Institute of Hygiene and Epidemiology, Prague, Czechoslovakia
TI - MONITORING THE OCCUPATIONAL EXPOSURE TO MUTAGENS - FACTS AND IDEAS (MEETING ABSTRACT).
SI - HERN/81/02647
SO - Eleventh Annual Meeting of the European Environmental Mutagen Society, July 6-11, 1981, Budapest, Hungary The Society, 1981.
LA - ENG
AB - The cytogenetic analysis of peripheral lymphocytes, which proved

to be a feasible bioindicator of genetic damage to somatic cells of workers occupationally exposed to mutagens may be used as a tool for checking acceptability of MAC levels established for them in work environment. This approach was verified on groups exposed to dimethyl formamide, epichlorohydrin, epoxyresins, haloethers, hydrocarbons, styrene, vinyl chloride. A possible antimutagenic effect of vitamins was checked on the group treated by the ascorbic acid, its influence to the chromosome aberrations frequency is presented. The examination of mitotic index and blastic transformation in lymphocytes as well as Hb alkylation in RBC seems to be the necessary part of genetic monitoring, if individual risk should be evaluated. (no Refs)

114 AU - Bendix S
AD - Bendix Environmental Research, Inc., San Francisco, CA
TI - FIREFIGHTER EXPOSURE TO ORGANIC CARCINOGENS (MEETING ABSTRACT).
SI - HERN/81/02123
SO - J Occup Med; 23(4):305 1981
LA - ENG
AB - Burn, acute cardiac and respiratory hazards have been the past focus of attention to medical problems of firefighters. Firefighters are exposed to complex chemical mixtures of vaporized, off-gassed, decomposed and newly synthesized organic chemicals under conditions where they rarely know what they are breathing or what special chemicals hazards they may encounter. Self-contained breathing apparatus may not be worn, may not be available, or may not be properly maintained to preserve designed function. It is time to look at the long-term consequences of firefighter exposure to vinyl chloride, dioxins, urethane, benzene, tetrachloroethane, polyaromatic hydrocarbons and other carcinogens. Record-keeping and medical follow-up need improvement. (no Refs)

115 AU - Serrentino R ; Gervasi PG
AD - Laboratorio di Mutagenesi e Differenziamento, C.N.R., Pisa, Italy
TI - PHOTOMETRIC DETERMINATION OF MICROSOMAL EPOXIDE HYDROLASE ACTIVITY BY THE 4-(P-NITROBENZYL)PYRIDINE TEST.
SI - ICOB/81/20440
SO - Boll Soc Ital Biol Sper; 56(22):2393-2397 1980
LA - ITA
AB - A simple photometric assay for the determination of the microsomal epoxide hydrolase activity by the 4-(p-nitrobenzyl) pyridine test is described. Microsomal epoxide hydrolase plays a key role in the detoxification of olefinic and aromatic hydrocarbons which are transformed into mutagenic and carcinogenic epoxides (such as vinyl chloride and benzo(a)pyrene) in the body. (8 Refs)

116 AU - Lijinsky W ; Andrews AW
AD - Chemical Carcinogenesis Program, Frederick Cancer Res. Center, Frederick, MD, 21901
TI - MUTAGENICITY OF VINYL COMPOUNDS IN SALMONELLA TYPHIMURIUM.
SI - ICDB/81/20063
SO - Teratogenesis Carcinog Mutagen; 1(3):259-267 1980
LA - ENG
AB - The mutagenic activities of 18 compounds that are structurally related to vinyl chloride were assayed in Salmonella typhimurium tester strains TA1535, TA1537, TA1538, TA98, and TA100 in the presence and absence of liver microsomal preparations. Ten compounds were nonmutagenic in all strains. Mutagenic activities in one or more strains were found, however, for acrolein, acrolein diethylacetal, allyl alcohol, acrylonitrile, allyl bromide, crotonaldehyde, crotyl alcohol, and vinyl bromide. (18 Refs)

117 AU - Fabricant JD ; Chalmers JH
AD - Dept. Preventive Medicine and Community Health, Univ. Texas Medical Branch, Galveston, TX, 77550
TI - EVIDENCE OF THE MUTAGENICITY OF ETHYLENE DICHLORIDE AND STRUCTURALLY RELATED COMPOUNDS.
SI - ICDB/81/14170
SO - Banbury Rep Ser; 5:309-329 1980
LA - ENG
AB - The short-term mutagenicity assays for ethylene dichloride (EDC) and its structural analogs are reviewed. The most widely used short-term mutagenicity tests are Salmonella mammalian microsome assay (Ames test), yeast or Neurospora, sex-linked recessive lethal mutation in Drosophila, or in vitro studies in cell culture. Positive results were reported for EDC, vinyl chloride, vinylidene chloride, and trichloroethylene, while perchloroethylene showed mutagenic activity in Salmonella and in Escherichia coli systems. (36 Refs)

118 AU - Infante PF ; Marlow PB
AD - Office of Carcinogen Identification and Classification, Occupational Safety and Health Admin., Washington, DC, 20210
TI - EVIDENCE FOR CARCINOGENICITY OF SELECTED HALOGENATED HYDROCARBONS INCLUDING ETHYLENE DICHLORIDE.
SI - ICDB/81/14169
SO - Banbury Rep Ser; 5:287-308 1980
LA - ENG
AB - The experimental and epidemiological studies on the carcinogenicity of 10 halogenated hydrocarbons related to vinyl chloride (VC) are reviewed. All 10 chemicals induced malignant tumors in both rats and mice. Liver was the target organ for 9/10 substances. Ethylene dichloride induced carcinomas of the forestomach and liver and adenocarcinomas of the mammary gland in both rats and mice, while spleen angiosarcomas were recorded only in rats. Ethylene dibromide induced tumors in the greatest number of organs. Analysis of cancer incidence among the workers exposed

to certain halogenated hydrocarbons suggested an elevated risk of lung cancer among the workers exposed to epichlorohydrin. (1 Ref)

119 AU - Johnson MN
AD - B. F. Goodrich Co., Akron, OH, 44318
TI - MEDICAL ASPECTS OF ETHYLENE DICHLORIDE IN THE WORKPLACE.
SI - ICDB/81/14166
SO - Banbury Rep Ser; 5:257-263 1980
LA - ENG
AB - The efficacy of regular periodic medical examination for workers exposed to ethylene dichloride (EDC) is discussed. It is emphasized that although a periodic medical examination can detect the early clinical signs of chronic exposure to certain chemicals (organophosphorous insecticides), it is quite useless for the evaluation of long-term effects of exposure to other chemicals such as vinyl chloride for which EDC is a raw material. (no Refs)

120 AU - Ames B ; Infante P ; Reitz R
AD - Dept. Biochemistry, Univ. California, Berkeley, CA
TI - ETHYLENE DICHLORIDE: A POTENTIAL HEALTH RISK?
SI - ICDB/81/14155
SO - Banbury Rep Ser. Vol. 5, 350 pp., 1980.
LA - ENG
AB - This vol contains the papers presented at the four sessions of a conference held to explore the potential carcinogenicity for humans of ethylene dichloride (EDC) and related halogenated hydrocarbons. The subjects of the individual sessions were the mutagenicity and carcinogenicity of EDC, toxicology and other topics, uses of EDC and worker exposure, and related chemicals. Although there is no evidence that EDC causes birth defects or reproductive effects, animal studies and Salmonella and Drosophila assays suggested that it may pose a carcinogenic and a mutagenic hazard. Of the other halogenated hydrocarbons discussed, vinyl bromide, vinly chloride and ethylene dibromide were described as being carcinogenic. Results of preliminary assessment of human exposure to EDC indicated that greater than 99% of the exposures are in the range of 10-990 parts per trillion. These results suggested that the relative human risk is low. (332 Refs)

121 AU - Sokal JA ; Baranski B ; Majka J ; Rolecki R ; Stetkiewicz J
AU - Ivanova-Chemishanska L ; Vargieva T ; Antonov G ; Mirkova E
AU - Kolakowski J ; Szendzikowski S ; Wroblewska K
AD - Inst. Occupational Medicine, P. O. Box 199, 90-950 Lodz, Poland
TI - EXPERIMENTAL STUDIES ON THE CHRONIC TOXIC EFFECTS OF VINYL CHLORIDE IN RATS.
SI - ICDB/81/13393
SO - J Hyg Epidemiol Microbiol Immunol (Praha); 24(3):285-294 1980
LA - ENG
AB - The time course of chronic toxic effects of vinyl chloride (VC) in Wistar rats was investigated. Rats were exposed in dynamic inhalation chambers to VC at concentrations of 50 ppm, 500 ppm,

and 20,000 ppm for 10 mo, 5 hr/day, 5 days/wk. Apparent treatment-related pathomorphological changes developed in the liver and testes; the liver changes appeared earlier and at lower VC concentrations than the testicular changes. Body wt decreased in the VC-treated rats. These changes increased with the duration of exposure. Increased relative wt of some organs and slight hematological and biochemical changes in blood during the course of the experiment also were observed. Even at the lowest VC concentration, some toxic effects were observed, including depression of body wt increase, increased relative wt of some internal organs, slight hematological and biochemical changes and fluctuations, and ultrastructural changes in hepatocytes and the tendency for an increased incidence of histological liver changes. Based on the assumption that 50 ppm is the threshold concentration of VC for rats, a level of 5 ppm was estimated to be the safe exposure limit in industry with respect to systemic effects. (27 Refs)

122 AU - Tarkowski S ; Wisniewska-Knypl JM ; Klimczak J ; Draminski W
AU - Wroblewska K
AD - Div. Industrial Toxicology, Inst. Occupational Medicine, ul. Teresy 8, 90-950 Lodz, Poland
TI - URINARY EXCRETION OF THIODIGLYCOLLIC ACID AND HEPATIC CONTENT OF FREE THIOLS IN RATS AT DIFFERENT LEVELS OF EXPOSURE TO VINYL CHLORIDE.
SI - ICOB/81/13895
SO - J Hyg Epidemiol Microbiol Immunol (Praha); 24(3):253-261 1980
LA - ENG
AB - Male Wistar rats were exposed to vinyl chloride (VC: 50, 200, 500, 1,000, or 20,000 ppm) one time for 5 hr or for 6 mo (5 hr/day/5 days/wk), and the oxidation of inhaled VC was assessed by measuring the urinary excretion of thiodiglycollic acid (TDGA). The conjugation of VC metabolites was assessed by measuring the hepatic contents of nonprotein thiols. The rate of urinary excretion of TDGA after VC exposure depended on the activity of microsomal monooxygenase. TDGA was found in the urine 24 hr after exposure to 50 ppm VC; urine excretion of TDGA increased with increasing VC exposure. In general, there were no significant differences in TDGA excretion in rats exposed to either single or long-term exposure, except that a 6-mo exposure to 20,000 ppm VC resulted in a lowered TDGA excretion compared to that observed after a single 20,000-ppm exposure. Excretion of TDGA in exposed rats was accompanied by a depression in the nonprotein thiol content in the liver. Pretreatment of the rats with an inducer or inhibitor of cytochrome P-450 synthesis resulted in an increase or complete inhibition, respectively, of TDGA excretion. Pretreatment of rats that had been exposed to 20,000 ppm VC with either phenobarbital or CoCl2 increased the nonprotein sulfhydryl hepatic content (6.0 +-0.3 or 8.4 +-0.4 micromoles (umoles)/g liver, respectively), compared to rats that had been exposed to 20,000 ppm VC alone (2.8 +-0.3 umoles/g). Glutathione reductase levels in umoles sulfhydryl/g liver/15 min were 126 +-6, 209 +-21, and 167 +-13 for rats exposed to

20,000-ppm VC only, for VC plus phenobarbital pretreatment, and for VC plus CoCl2 pretreatment, respectively. (20 Refs)

123 AU - Hanawa K ; Yamada S ; Suzuki H ; Nagayo T
AD - First Dept. Pathology, Aichi Cancer Center, Chikusa-ku, Nagoya 464, Japan
TI - EFFECTS OF SODIUM CHLORIDE ON GASTRIC CANCER INDUCTION BY N-METHYL-N'-NITRO-N-NITROSOGUANIDINE (MNNG) IN RATS (MEETING ABSTRACT).
SI - ICDB/81/10700
SO - Proceedings of the 39th Annual Meeting of the Japanese Cancer Association held in Tokyo, 5-7 November, 1980. The Japanese Cancer Association, Tokyo 170, Japan, 367 pp., 1980.
LA - JPN
AB - Seven-wk-old male and female Wistar rats (WBN/Kob) were given a saturated aqueous NaCl soln with N-methyl-N'-nitro-N-nitrosoguanidine (MNNG; Group 1), NaCl at 50% saturation with MNNG (Group 2), MNNG alone (Group 3) or the saturated saline soln alone (Group 4). The saline soln (1 ml) was administered through a vinyl tube once a wk and 25 mg of MNNG per liter was added to the drinking water daily, both for 20 wk. The rats were then given tap water to drink and examined. Gastric cancers were produced in 1/4, 4/7, 0/10 and 0/7 of the male rats, and in 4/11, 4/7, 2/8 and 0/7 of the female rats, in Groups 1, 2, 3, and 4, respectively. The incidence of gastric tumors was higher in the groups given MNNG + a saline soln than in the group given MNNG alone, and the group given the 50% saturated saline soln had a higher incidence of gastric tumors than the group given the saturated saline soln in both males and females. The incidence of cancer in the rats given both MNNG and a saline soln did not differ significantly with the sex of the rats, but tumors were produced only in the female rats when MNNG was administered alone. Most of the tumors were restricted to the pyloric area (11/15) and they were histologically highly atypical adenoma (3/15) or well-differentiated adenocarcinoma (12/15). In conclusion, NaCl was found to have a promotive effect on MNNG-induced gastric cancer. (no Refs)

124 AU - Veltman G
AD - Universitatshautklinik, Sigmund-Freud-Str. 25, D-5300 Bonn 1, W. Germany
TI - CLINICAL FINDINGS AND ASPECTS OF OCCUPATIONAL MEDICINE IN VINYL CHLORIDE DISEASE.
SI - ICDB/81/10018
SO - Dermatol Monatsschr; 166(11):705-712 1980
LA - GER
AB - Symptoms caused by long-term exposure to vinyl chloride (VC) are reviewed, and health risks (including cancer) associated with VC exposure are discussed. Physical properties of VC are briefly outlined, and industrial occupations in which workers risk exposure to this chemical are noted. Effects of long-term exposure to VC are described with respect to clinical manifestations, scintigraphic and roentgenologic findings, and

laboratory findings; the relative incidence of the most frequent symptoms is noted. Paraclinical findings in patients with long-term VC exposure are discussed with respect to changes in skin, alterations in blood vessels or bone, liver damage, and chromosome anomalies. The possibility that VC exposure results in CNS symptoms is considered. The course of VC-caused symptoms is described for patients with continued exposure to VC and patients for whom VC exposure is eliminated; emphasis is placed on the reversal of many symptoms in patients no longer exposed to VC. In consideration of the potential health effects of VC, measurement of VC damage and limits of VC exposure are discussed. The relationship between VC exposure and the development of angiosarcoma is noted. (52 Refs)

125 AU - Krajewski J ; Dobecki M ; Gromiec J
AD - Dept. Chemical Air Pollutants, Inst. Occupational Medicine, Lodz, Poland
TI - RETENTION OF VINYL CHLORIDE IN THE HUMAN LUNG.
SI - ICOB/81/09869
SO - Br J Ind Med; 37(4):373-374 1980
LA - ENG
AB - Experiments with volunteers showed that 42% of an inhaled dose of vinyl chloride is retained in the lungs. This value is independent of the concentration of vinyl chloride in the air. Elimination of vinyl chloride through the lungs is negligible since its concentration in expired air decreases immediately after the cessation of exposure. (Author abstract) (4 Refs)

126 AU - Natarajan AT ; Obe G
AD - Dept. Radiation Genetics and Chemical Mutagenesis, Silvius Laboratories, Univ. Leiden, Wasenaarseweg 72, Leiden, The Netherlands
TI - SCREENING OF HUMAN POPULATIONS FOR MUTATIONS INDUCED BY ENVIRONMENTAL POLLUTANTS: USE OF HUMAN LYMPHOCYTE SYSTEM.
SI - ICOB/81/09352
SO - Ecotoxicol Environ Saf; 4(4):468-481 1980
LA - ENG
AB - The frequencies of chromatid gaps (G) and breaks (B'), isochromatid/chromosome breaks (B''), chromatid translocations (RB'), dicentrics (DIC), rings, balanced translocations (BT), and inversions (INV) in phytohemagglutinin-stimulated 48-hr peripheral blood lymphocyte (PBL) cultures may be a useful means of monitoring exposure to environmental mutagens and carcinogens. In a 72-hr PBL culture, the cells are in the second or third metaphase and many chromosome aberrations have been lost. The reported av frequency of exchange-type aberrations (DIC, RB', and rings) in 48-hr PBL cultures is 9.64(4) metaphases. The reported frequencies of gaps, B', and B'' are higher and vary widely, perhaps because different criteria may be used to distinguish them. In the PBL of irradiated persons (Hiroshima and Nagasaki residents or patients given radiotherapy for ankylosing spondylitis), the frequencies of DIC and rings decline with time, but reciprocal translocations persist at an unchanged high

frequency for many yr. Increased frequencies of exchange-type aberrations (DIC, rings, and RB') and breaks (B' and B") have been reported in the PBL of alcoholics, heavy smokers, and workers exposed to high concentrations of vinyl chloride and other mutagens. Infectious hepatitis and mononucleosis also increase the frequency of chromosomal aberrations, but the long-term persistence of these effects is unknown. The frequencies of micronuclei and hypoxanthine guanine phosphoribosyltransferase deficiency (associated with 6-thioguanine resistance) in normal PBL are low. These criteria may be useful for assessing environmental mutagen/carcinogen exposure in vivo. Assays of sister chromatid exchange frequencies do not seem to be suitable for this purpose. (25 Refs)

127 AU - Lilis R
AD - Environmental Sciences Lab., Mt. Sinai Sch. Medicine, New York, NY, 10029
TI - VINYL CHLORIDE AND POLYVINYL CHLORIDE EXPOSURE AND OCCUPATIONAL LUNG DISEASE.
SI - ICCB/81/07950
SO - Chest; 78(6):826-828 1980
LA - ENG
AB - Epidemiologic studies concerning the harmful effects of vinyl chloride (VC) and polyvinyl chloride (PVC) on humans are reviewed. The effects of VC or PVC on the respiratory system of exposed workers seem to indicate two patterns of nonmalignant effects: 1) a granulomatous reaction to PVC dust with inclusion of PVC particles in macrophages and histiocytes and associated interstitial fibrosis; and 2) an interstitial pulmonary fibrosis caused by VC interacting with protein molecules and the immunologic mechanisms triggered by the altered protein. Long-term effects include carcinogenicity. There is an increased incidence of lung cancer in exposed populations, and mice exposed to VC have developed hyperplastic changes of the alveolar lining cells and pulmonary tumors. An ultrastructural examination of these murine tumors seems to indicate that the tumors originated in type 2 alveolar cells. The magnitude of the carcinogenic effects of VC on humans has not yet been completely evaluated. (22 Refs)

128 AU - Selikoff IJ
AD - Environmental Sciences Lab., Mount Sinai Sch. Medicine, City Univ. New York, 10 East 102 St., New York, NY, 10029
TI - CHEMICAL DISEASE IN HUMANS: PROBLEMS IN COMPARATIVE TOXICOLOGY.
SI - ICCB/81/07193
SO - Ciba Found Symp; 76:331-347 1980
LA - ENG
AB - Since the latent periods for human tumors induced by such chemicals as vinyl chloride, Thorotrast, beta-naphthylamine, benzidine, and asbestos may be 20-30 yr, the carcinogenic potentials of more recently introduced xenobiotics (eg, polychlorinated biphenyls, polybrominated biphenyls, or dioxin) cannot yet be determined. Xenobiotics may persist and accumulate

in tissue stores. Some chemicals may seemingly disappear from the body, but leave a tissue imprint of their effects that appears decades after exposure ceases. Estimates of biologically active doses are sometimes complicated by the presence of highly toxic trace contaminants and homologs of varying biologic activities. The effects of chemical exposure on the tissues may be obscured by the absence of the characteristic symptoms normally associated with the disease. The lack of coherence between laboratory results and the clinical effects of enzyme-inducing agents may be explained by interactions between two or more xenobiotics or between the chemical(s) and genetic or metabolic variables. Since there is much evidence that biologic processes are strikingly similar in different mammalian species, the toxicologic significance to humans of enzyme induction and related processes requires careful evaluation. (22 Refs)

129 AU - Wagoner JK ; Infante PF ; Apfeldorf RB
AD - Environmental Defense Fund, Washington, DC
TI - TOXICITY OF VINYL CHLORIDE AND POLYVINYL CHLORIDE AS SEEN THROUGH EPIDEMIOLOGIC OBSERVATIONS.
SI - ICDB/81/95390
SO - J Toxicol Environ Health; 6(5/6):1101-1107 1980
LA - ENG
AB - Epidemiologic evidence of the carcinogenicity of vinyl chloride (VC) and polyvinyl chloride (PVC) is reviewed. Occupational exposure to VC has been associated with an increased risk of liver cancer. Cases of liver angiosarcoma have been reported in association with exposure to VC throughout the world. Apparent neoplastic changes in the livers of rats have been observed after the administration of VC monomers (as PVC powder in the diet) at levels of 3 and 9 mg/kg body wt. Both experimental bioassay and epidemiologic study have demonstrated that the brain is a target organ for the carcinogenicity of VC. Evidence supporting the association of VC exposure and pneumoconiosis is presented. Studies are reviewed which suggest that the excess lung cancer risk in the VC-PVC industry is related to exposure to PVC dust, which is either a carrier of residual VC monomers or is itself a factor in the etiology of lung cancer. It is also possible that PVC dust particles in the lung slowly release VC monomer to small adjacent areas of the tissue, thereby prolonging contact with the chemical. More data are needed to demonstrate an association between VC and cancers of the lymphatic system. (23 Refs)

130 AU - Axelson O
AD - Dept. Occupational Medicine, Univ. Hosp., Linkoping, Sweden
TI - CHLORINATED HYDROCARBONS AND CANCER: EPIDEMIOLOGIC ASPECTS.
SI - ICDB/81/95383
SO - J Toxicol Environ Health; 6(5/6):1245-1251 1980
LA - ENG
AB - Clinical and epidemiologic data on the carcinogenic properties of the more important halogenated hydrocarbons are reviewed. Mutagenic and carcinogenic properties have been reported for pesticides such as lindane, chlordane, phenoxy acids, and various

chlorophenols. Chlorinated solvents (CCl4, trichloroethylene, methylchloroform, and methyl chloride) have been shown to be carcinogenic in animals, but similar epidemiologic evidence is limited. Both chloromethyl methyl ether and bischloromethyl ether are potent cancer initiators in animals. Vinyl chloride has been mentioned as a probable cause of liver angiosarcoma in exposed workers and may be the cause of other cancers. An excess of reticuloendothelial and lymphoid malignancies has been reported among anesthesiologists. The occurrence of trihalomethanes in drinking water has been associated with increased cancer in the general population including bladder cancer, brain tumors, kidney cancers, and non-Hodgkin's lymphomas. There is an urgent need for adequately designed epidemiologic studies. While bacterial test systems and animal experiments demonstrate the mutagenic and carcinogenic properties of these substances, few have been conclusively associated with human cancer. (62 Refs)

131 AU - Bogovski P
AD - Inst. Experimental and Clinical Medicine, Ministry Health Estonian SSR, Tallinn, USSR
TI - HISTORICAL PERSPECTIVES OF OCCUPATIONAL CANCER.
SI - ICDB/81/95320
SO - J Toxicol Environ Health; 6(5/6):921-939 1980
LA - ENG
AB - The present state and possible future trends of occupational cancer, some lessons from the past, and the potential input from experimental research are reviewed. The most important occupational carcinogens are asbestos and vinyl chloride. The problems of N-nitroso compounds (approx 80% of which have induced cancer in various species and organs) are discussed. In addition to the main cancer site associated with an occupational carcinogen, cancers at other sites appear more frequently. The controversy over the proportion of cancers related to occupation in the overall cancer incidence is discussed. Epidemiological studies, the proper functioning of health services, and prevention, all depend on adequate registration of cancer cases. Skin cancer caused by oil is reviewed in detail. Experimental data should be accepted as sufficient to warrant beginning preventive measures. The multifactorial etiology of occupational cancers is discussed. Experimental cancer research is discussed with respect to life-style and modifying factors acting on the penetration of a carcinogen into target cells. Future tasks and goals are discussed. (95 Refs)

132 AU - National Toxicology Program
AD - U. S. Public Health Service, Washington, DC
TI - FIRST ANNUAL REPORT ON CARCINOGENS (JULY 1980).
SI - ICDB/81/94580
SO - First Annual Report on Carcinogens (July 1980). Bethesda, MD, Department of Health and Human Services, Vol. 1, 150 pp., 1980.
LA - ENG
AB - This report, from the National Toxicology Program, discusses a group of 26 IARC-reviewed chemicals and industrial processes

initially found associated with the induction of human cancer. Data are included on exposure environments, and the status of existing regulations of these chemicals. The group includes: aflatoxin, 4-aminobiphenyl, arsenic and inorganic arsenic compounds, asbestos, auramine, benzene, benzidine, N,N-bis(2-chloroethyl)-2-naphthylamine, bis(chloromethyl)ether, cadmium and cadmium compounds, chloramphenicol, chloromethyl methyl ether, chromium and chromium compounds, cyclophosphamide, diethylstilbestrol, hematite and iron oxides, isopropyl oils, melphalan, mustard gas, 2-naphthylamine, nickel and nickel compounds, oxymetholone, phenacetin, phenytoin and phenytoin sodium, soots, tars, oils, and vinyl chloride. (no Refs)

133 AU - Heng CB ; Winston JM ; Lee CC
AD - Midwest Res. Inst., Kansas City, MO
TI - ANIMAL MODEL: ANGIOSARCOMA OF RATS AND MICE INDUCED BY VINYL CHLORIDE.
SI - ICDB/81/94564
SO - Am J Pathol; 101(3):737-740 1980
LA - ENG
AB - Hepatic angiosarcoma may develop in humans exposed to vinyl chloride (VC), thorotrast, and arsenic. In man, liver is the only organ affected by VC. Hepatocellular carcinoma is the only tumor besides hepatic angiosarcoma suspected to be associated with VC exposure. The animal model for the study of angiosarcoma in man adds another reproducible system to the study of tumorigenesis, treatment, and prevention of neoplasms. (10 Refs)

134 AU - Sharma RP ; Yakel HO ; Gehring PJ
AD - Dept. Animal, Dairy, and Veterinary Sciences, Utah State Univ., UMC 56, Logan, Utah, 84322
TI - IMMUNOTOXICOLOGIC STUDIES WITH VINYL CHLORIDE IN RABBITS AND MICE.
SI - ICDB/81/94297
SO - Int J Immunopharmacol; 2(4):295-299 1980
LA - ENG
AB - Immunologic responses to inoculated antigens were studied in rabbits exposed to vinyl chloride (VC), and the effects of two known major metabolites of VC were observed in vitro in mouse splenic cells. New Zealand rabbits were exposed to 0 (control), 10, 100, or 1,000 ppm VC, 6 hr/day, 5 days/wk, for 8 wk in inhalation chambers. After 4 wk of exposure, the animals were injected in the footpads with an antigen containing a 1:1 mixture of tetanus toxoid and Freund's complete adjuvant; the injection was repeated 2 wk later. No effect of this treatment was noted when the body wt and wt of various organs (kidneys, brain, heart, spleen, adrenals, and popliteal lymph nodes) of treated and control rabbits were compared; however, thymus wt showed a dose-related increase in rabbits treated with the two highest doses of VC. Various tests of antigen-induced immune responses in VC-exposed rabbits revealed no treatment-related effects. The incorporation of 3H-thymidine in splenic lymphocyte cultures of immunized and VC-exposed rabbits was very high, even in the absence of mitogens; this finding was consistent with that

generally observed in immunized animals. Exposure to 10 or 100 ppm VC further increased this spontaneous transformation, while exposure to 1,000 ppm VC produced a decrease. Incubation of mouse splenic lymphocyte cultures in the presence of thiodiglycolic acid (TDGA) or N-acetyl-S-(hydroxyethyl)-cysteine did not suggest a definite effect. In contrast, when TDGA was given to mice in their drinking water, there was a dose-related increase in the splenic lymphocyte transformations. (10 Refs)

135 AU - Cohen LF ; Ewig RA ; Kohn KW ; Glaubiger D
AD - Pediatric Oncology Branch, Div. Cancer Treatment, NCI, NIH, Bethesda, MD, 20205
TI - INTERSTRAND DNA CROSSLINKING BY 4,5',8-TRIMETHYLPSORALEN PLUS MONOCHROMATIC ULTRAVIOLET LIGHT. STUDIES BY ALKALINE ELUTION IN MOUSE L1210 LEUKEMIA CELLS.
SI - ICDB/81/94260
SO - Biochim Biophys Acta; 610(1):56-63 1980
LA - ENG
AB - DNA crosslinking by 4,5',8-trimethylpsoralen plus monochromatic UV light of wavelength 365 nm was studied in mouse L1210 leukemia cells. DNA breaks and crosslinking were evaluated by alkaline elution of DNA from poly(vinyl chloride) filters. Trimethylpsoralen plus 365 nm light produced DNA crosslinks but not breaks. The kinetics of crosslinking were linear with respect to concentration and second-order with respect to light exposure time. The latter finding supports the proposed two photon mechanism for the formation of diadducts. In contrast to DNA crosslinking agents such as nitrogen mustard, nitrosoureas and platinums, trimethylpsoralen crosslinks were resistant to proteolytic digestion. Thus, trimethylpsoralen plus 365 nm light produced interstrand crosslinks, as proposed for a bifunctional agent binding to bases on opposite DNA strands. (Author abstract) (29 Refs)

136 AU - Smith AH ; Waxweiler RJ ; Tyroler HA
AD - Dept. Community Health, Wellington Clinical Sch. Medicine, Wellington Hosp., Wellington 2, New Zealand
TI - EPIDEMIOLOGIC INVESTIGATION OF OCCUPATIONAL CARCINOGENESIS USING A SERIALLY ADDITIVE EXPECTED DOSE MODEL.
SI - ICDB/81/94125
SO - Am J Epidemiol; 112(6):787-797 1980
LA - ENG
AB - The epidemiologic identification of occupational carcinogens is complicated by several problems including worker mobility between jobs, variation over time of chemicals and processes used, and the long latency period between exposure and discovery of a tumor. In the light of these problems, a method using the cumulative dose concept has been developed which involves calculating the expected yearly exposure for each case from work histories of all noncases close to the case in yr of birth and yr of hire. The data required for use of the method include information concerning exposure to the chemicals being studied for each job in each calendar yr of the study. Use of the method

is illustrated with a study of angiosarcoma of the liver and vinyl chloride exposure in a polymerization plant. The value of the method lies in the wealth of information generated concerning the association between chemical exposures and cancer, including exposure level relationships, latency information, and the possibility that two chemicals might be acting independently or jointly. The serially additive expected dose model is likely to prove particularly useful in the analysis of data collected by occupational health surveillance systems, as well as retrospective studies of the type illustrated. (Author abstract) (18 Refs)

137 AU - Rossner P ; Sram RJ ; Novakova J ; Lambl V
AD - Inst. Hygiene and Epidemiology, 100 42 Prague, Czechoslovakia
TI - CYTOGENETIC ANALYSIS IN WORKERS OCCUPATIONALLY EXPOSED TO VINYL CHLORIDE.
SI - ICDB/81/93912
SO - Mutat Res; 73(2):425-427 1980
LA - ENG
AB - Chromosome analysis was done on lymphocytes obtained in 1977 and 1 yr later from 31 males (25-55 yr) exposed to 10 mg/cubic meter (m3) of vinyl chloride monomer (VCM) in air at the workplace, and compared with 35 controls not exposed to VCM. The analyses were done for four categories of chromosomal damage: chromatid and chromosome breaks, and chromatid and chromosome exchanges. Cells carrying breaks and/or exchanges were classified as aberrant (AB). To compare intergroup differences the relative frequencies of AB and 95% confidence limits were calculated. The relative frequencies were compared using the Gaussian t test (t5% = 1.96). In all subjects, only breaks were detected. No significant differences were found either between VCM-exposed groups and matching controls (VCM-1977 vs control, t = 1.52; VCM-1978 vs control, t = 0.25) or between the first and second sample collections (t = 1.83). These results showed that if the VCM concentration in the air of the workplace is kept less than 10 mg/m3, no increase should develop in the number of chromosome aberrations detectable in peripheral lymphocytes of these VCM-exposed workers. (12 Refs)

138 AU - Ebihara I ; Yoshizawa K
AD - Div. Work Environment and Occupational Diseases, Inst. for Science of Labor, Tokyo, Japan
TI - THREE CASES OF LUNG CANCER AMONG POLYVINYL CHLORIDE (PVC) WORKERS.
SI - ICDB/81/91911
SO - Rodo Kagaku; 56(10):577-585 1980
LA - JPN
AB - Patient 1, a 47-yr-old man with a 27-yr history of working in a vinyl sheet factory, had complaints of general malaise accompanied with 40 C fever, vomiting, coughing, chest pain, and pain in the right shoulder blade. The patient had been smoking 15 cigarettes/day for greater than 20 yr. Chest x-rays showed atelectatic change, constrictive pulmonitis, and a tumorous swelling of the right hilar area. The patient underwent surgical

resection of the tumor with a diagnosis of epidermoid cancer. Patient 2, a 50-yr-old man with an 8-yr history of working as a polyvinyl chloride and vinyl chloride monomer (VCM) plastics caster and a 25-yr history of smoking 12 cigarettes/day, was found to have a tumorous shadow in the region of the heart and lateral pleura with x-ray examination. The patient died prior to treatment for an adenocarcinoma. Autopsy showed small dust maculae, dust decomposition around vessels and bronchioles, and slightly thickened and fibrosed bronchiolar walls. Patient 3, a 47-yr-old man who worked as a plastics caster for 9 yr, had a history of smoking 10 cigarettes/day for 25 yr. The histological type of the tumor in Patient 3 was unknown. All three primary lung cancers were considered to be due to low grade occupational exposure to VCM and/or vinyl dichlorides. (37 Refs)

139 AU - Daudel R
AD - Universite Pierre et Marie Curie
TI - CONQUERING CANCER: PREVENTION AND TREATMENT.
SI - ICDB/81/91009
SO - Rev Palais Decouverte; 8(80):4-37 1980
LA - FRE
AB - The prevention of cancer, along with its etiology, diagnosis, and treatment are discussed. The importance of a balanced diet (80 g of fats, 100 g of proteins, and 300 g of carbohydrates for a total of 2,400 calories) and exercise in the prevention of cancer is emphasized. The carcinogenicity of certain foods and methods of food preparation (smoked fish and meat) are discussed. Geographic differences in cancer incidence as related to dietary habits are described. It is suggested that alcohol consumption predisposes a person to liver cancer. Abstinence from cigarette smoking was suggested in view of the correlation between smoking and bronchial and pulmonary cancer. Signs of aerodigestive, urinary cancer, gynecological, and breast cancer are discussed. Breast self-examination is described. The relationship between sunbathing and skin cancer is discussed. Leukemia, lymphoma, and cancers of the bone and nervous system are discussed. The hereditary nature of cancer is considered. The development of neoplasms and their metastasis are discussed. Carcinogenic compounds, such as benzene, benzopyrene, and vinyl chloride, and their effect on DNA are discussed. The role of radiation, viruses and other agents in cancer production is described. Methods of cancer diagnosis are described. Cancer therapy includes surgery, chemotherapy, radiotherapy, and immunotherapy. (10 Refs)

140 AU - Darnis F
AD - Universite Paris VI, Paris, France
TI - THE ROLE OF DIET IN THE PRODUCTION OF PRIMARY LIVER CANCER AND CERTAIN OTHER HUMAN CANCERS.
SI - ICDB/81/91393
SO - Rev Palais Decouverte; 8(80):38-51 1980
LA - FRE
AB - Three important food agents hepatocarcinogenic in humans are mycotoxins, nitrosamines, and halogenic ethylenes. In geographic

areas where consumption of aflatoxin B1-contaminated food is high there is greater incidence of liver cancer. Other mycotoxins, such as sterigmatocystines, luteoskyrines, and cyclochlorotines, have been shown to be carcinogenic in animals. Nitrosamines, found in fish, meats, alcoholic beverages, and tobacco smoke, have been shown to be hepatocarcinogenic in animals. The hepatocarcinogenicity of foods treated with nitrites, nitrates, or gluconodeltalactones is discussed. The formation of the nitrosamines in the human gastrointestinal tract is discussed. The hepatocarcinogenicity of halogenic ethylenes, especially vinyl chloride, is discussed. Workers exposed to vinyl chloride have been shown to develop liver angiosarcomas. The hepatocarcinogenicity of natural substances (pyrrolizidine alkaloids), environmental pollutants (DDT, polychlorinated biphenyls, chloroform), food dyes, and other agents (amitrol, diallate, bis(2-chloroethyl)ether, dimethoxan, and dioxan) is discussed. The role of polycyclic hydrocarbons in smoked meat and other foods in the production of digestive cancer is discussed. Pharyngeal and esophageal neoplasms are discussed in relation to alcohol intake and tobacco smoking. The role of dietary fats in colon, breast, and prostate cancer is discussed. (no Refs)

141 AU - Harrison EA
AD - Natl. Technical Information Service, Springfield, VA
TI - TOXICITY OF VINYL CHLORIDE. CITATIONS FROM THE NTIS DATA BASE.
SI - ICDB/81/91385
SO - Aerosp Med Biol; (211):215 1980
LA - ENG
AB - Research is cited on the health hazards from exposure to vinyl chloride and vinyl chloride resins. Studies are included on the epidemiology of industrial and public exposures to the compound and its degradation and combustion products. This updated bibliography contains 90 abstracts, 8 of which are new entries to the previous edition. (Author abstract) (no Refs)

142 AU - Daune M ; Fuchs PP
AD - Departement de Biophysique, Universite Louis Pasteur, Strasbourg, France
TI - CHEMICAL CARCINOGENESIS.
SI - ICDB/81/91051
SO - Recherche; 11(115):1066-1077 1980
LA - FRE
AB - The chemical causes of cancer are reviewed. The historical significance of scrotal cancer in chimney sweeps is discussed. The list of known chemical carcinogens includes polycyclic hydrocarbons, benzene, and vinyl chloride. Chemical carcinogens affect the DNA of the cell by lysing the double strands and by causing modifications in the genetic information. These modifications lead to a decreased stability in the DNA molecules and to constraints which force the unwinding of the double helix such that there are resulting denatured zones. Chemical carcinogens are capable of causing direct and indirect mutations. In order for cancer to develop, the first initiation stage must

be followed by a promotion stage. (9 Refs)

143 AU - Krajewski J ; Milczarska A ; Dobecki M
AD - Zaklad Chemicznych Zanieczyszczen Powietrza, Instytut Medycyny Pracy, ul. Teresy 8, 90-950, Poland
TI - USEFULNESS OF DIFFERENT METHODS OF AIR SAMPLING FOR THE EVALUATION OF WORKERS' OCCUPATIONAL EXPOSURE TO VINYL CHLORIDE.
SI - ICDB/81/90845
SO - Med Pr; 31(3):165-170 1980
LA - POL
AB - The vinyl chloride (VC) concentrations were measured in a polymerization plant by different sampling methods (stationary sampling, FIDAS autoanalyzer, and individual sampling) to determine the exposure of the workers. The findings showed that the worker's exposure was estimated correctly only by air sampling in the breathing zone. The VC concentrations in the breathing zone were in the range of 1.8-209.5 mg/cubic meter. (7 Refs)

144 AU - Maclure KM ; MacMahon B
AD - Dept. Epidemiology, Harvard Sch. Public Health, 677 Huntington Ave., Boston, MA, 02115
TI - AN EPIDEMIOLOGIC PERSPECTIVE OF ENVIRONMENTAL CARCINOGENESIS.
SI - ICDB/81/90393
SO - Epidemiol Rev (Engl Transl Przegl Epidemiol); 2:19-48 1980
LA - ENG
AB - Current epidemiologic knowledge concerning the relationship between environmental agents and cancer is reviewed. Different uses of the word 'environment' are discussed, and problems that arise from the failure to appreciate these different uses are outlined. Environmental agents here include two classes: substances to which exposure is deliberate (consumables) and substances to which exposure is inadvertent (contaminants). Epidemiologic evidence for associations between cancer and consumables is discussed for: tobacco, alcohol, food (including fiber, fat, vegetables, essential nutrients, and nonnutrients such as coffee), drugs, and cosmetics. Epidemiologic evidence for associations between cancer and the following types of contaminants is summarized: contaminants in the workplace, including asbestos, metal compounds, vinyl chloride, alkylating agents, etc; pollutants in the air, water, and food outside the workplace; biologic contaminants, including viruses and mycotoxins; and physical contaminants, including UV and ionizing radiation. Some of the problems encountered in quantitation of environmental carcinogens are examined; emphasis is placed on problems of measuring dose, assessing response, determining latent period, identifying dose-response patterns, and considering the possible existence of threshold values and interactions between agents. (281 Refs)

145 AU - Ottenwalder H ; Bolt HM
AD - (c/o Bolt) Pharmakologisches Institut, Dusseldorf University, Obere Zahlbacher Str. 53, D-5600 Mainz, W. Germany
TI - METABOLIC ACTIVATION OF VINYL CHLORIDE AND VINYL BROMIDE BY ISOLATED HEPATOCYTES AND HEPATIC SINUSOIDAL CELLS.
SI - ICDB/81/90103
SO - J Environ Pathol Toxicol; 4(1):411-417 1980
LA - ENG
AB - Hepatocytes and sinusoidal cells were prepared from female Wistar rat liver, then separately incubated with 14C-labeled vinyl chloride (VC) or its analog, vinyl bromide (VB), to study the oxidative metabolism of vinyl chloride in the liver. Metabolic activation in each incubation was measured by determining the extent of covalent binding of metabolites to protein. The capability of sinusoidal cells to transform VC and VB to protein alkylating metabolites was less than that of hepatocytes, and was not detectable in some experiments. A lower alkylation rate of VB metabolites was also shown. The results showed that VC and VB are primarily metabolized within hepatocytes in rats. (13 Refs)

146 AU - Lazaris AYa ; Schmujlovich SM ; Kalmikova TA
AD - V. A. Kargin Inst. Polymer Chemistry and Technology, Dzerjinsk, Gorky District 606000, USSR
TI - DETERMINATION OF RESIDUAL VINYL CHLORIDE IN POLY(VINYL CHLORIDE) RESINS.
SI - ICDB/81/89652
SO - J Chromatogr; 198(3):337-346 1980
LA - ENG
AB - The determination of residual vinyl chloride (VC) in poly(vinyl chloride) (PVC) powders based on thermal desorbtion in a carrier gas stream and trapping of the VC is described. A trap is installed in the heated injection port of a gas chromatograph and desorbed volatiles are chromatographed by a two-stage chromatographic system. While VC is purged through an analytical column, the first column is cleaned by back-flushing. The method has been tested on various types of PVC powders and has no limit of sensitivity. (Author abstract) (31 Refs)

147 AU - Rogan WJ
AD - Biometry Branch, Natl. Inst. Environmental Health Sciences, P. O. Box 12233, Research Triangle Park, NC, 27709
TI - THE SOURCES AND ROUTES OF CHILDHOOD CHEMICAL EXPOSURES.
SI - ICDB/81/89468
SO - J Pediatr; 97(5):861-865 1980
LA - ENG
AB - Exposure conditions examined include: toxic chemicals carried home by parents returning from work, exposure of mother and fetus to toxic chemicals at the mother's place of employment, air pollution hazards, concentrations of toxic chemicals in mothers' milk, bioaccumulation of chemicals in lower stages of the food chain which in turn are ingested by humans, accumulation of chemicals in various parts of the human body, pollution in the

home particularly arising from renovations or inappropriate use of chemicals; and exposures of epidemic proportions resulting from accidental spillages, massive misuses of chemicals, or improper storage of chemical wastes. Specific references to cancer included the development of mesothelioma in children who had been playing in mine tailings around asbestos sites, the development of angiosarcoma following vinyl chloride exposure, and lung cancer in response to toxic irritants. (49 Refs)

148 AU - Boccelli JW ; Kerbekus BB
AD - Air Pollution Res. Lab., New Jersey Inst. Technology, Newark, NJ
TI - ANALYSIS OF SELECTED VOLATILE ORGANIC SUBSTANCES IN AMBIENT AIR.
SI - ICDB/81/88320
SO - Analysis of Selected Volatile Organic Substances in Ambient Air. Available from National Technical Information Service, Springfield, Va,, as PB80-144694:, N80-26960, NJDEP-79/02, HC A05/MF A01 CSCL 07D, 80 pp., 1980.
LA - ENG
AB - Sampling/analytical methodologies and laboratory techniques in determining the concentrations of selected volatile organic substances in the vapor phase are described. A total of 330 samples from northern New Jersey were collected. The samples were then analyzed for benzene, carbon tetrachloride, chloroform, o-dichlorobenzene and p-dichlorobenzene, 1,2-dichloroethane, nitrobenzene, tetrachloroethylene, 1,1,1-trichloroethane, trichloroethylene, and vinyl chloride. Full data sets for all samples are appended to the report. (Author abstract)

149 AU - Moore EC
AD - No affiliation given
TI - WOMEN AND HEALTH ISSUES: OTHER HEALTH CONCERNS.
SI - ICDB/81/88214
SO - Public Health Rep; 95(Suppl):33-47 1980
LA - ENG
AB - Environmental, occupational, and cultural conditions associated with carcinogen exposure among women are reviewed. More than 90% of all hairdressers and beauticians are women, and many aerosol sprays used by such workers in the past have contained vinyl chloride, a liver carcinogen. Many hair dyes have been shown to be mutagenic. Women comprise 56% of the textile worker population, and exposure to asbestos-containing textile products may lead to the development of lung and other types of cancer. Women account for almost two-thirds of the workers in the laundry and dry cleaning industry, and dry cleaning workers are exposed to solvents such as perchloroethylene, which has been linked to cancer in animal studies. Cultural habits associated with carcinogen exposure among women include increased cigarette smoking and the use of cosmetics. (45 Refs)

150 AU - Baxter PJ ; Anthony PP ; Macsween RN ; Scheuer PJ
AD - Employment Medical Advisory Service, London NW1 5DT, England
TI - ANGIOSARCOMA OF THE LIVER: ANNUAL OCCURRENCE AND AETIOLOGY IN GREAT BRITAIN.
SI - ICDB/81/87442
SO - Br J Ind Med; 37(3):213-221 1980
LA - ENG
AB - The annual occurrence of angiosarcoma of the liver (ASL) in Britain from 1963 to 1977 was studied, including clinical and occupational details for those cases agreed as ASL by a panel of histopathologists. Thirty-five cases (28 men, 6 women, and 1 infant girl) were agreed as ASL. The increase in the incidence of ASL observed in recent yr was attributable to Thorotrast (thorium dioxide) usage (8 cases) and exposure to vinyl chloride (2 cases) in the past. In its clinical presentation and prognosis ASL resembled primary liver carcinoma, except that extrahepatic metastases were found in only eight (23%) cases, and hemoperitoneum was more common in these cases due to Thorotrast. The results suggested a possible increased risk of ASL in the electrical and plastics fabrication industries, but information on exposure was inadequate to implicate specific chemicals. The clinical features of one case were indicative of arsenical intoxication, but medications in the other patients did not appear to be of etiological importance. (Author abstract) (32 Refs)

151 AU - Harrison EA
AD - Natl. Technical Information Service, Springfield, VA
TI - TOXICITY OF VINYL CHLORIDE (CITATIONS FROM THE NTIS DATA BASE).
SI - ICDB/81/87218
SO - Toxicity of Vinyl Chloride (Citations from the NTIS Data Base). Available Through National Technical Information Service, Springfield, Va,, as PB80-807662:, PB80-807662, 97 pp., 1980.
LA - ENG
AB - Research is cited on the health hazards from exposure to vinyl chloride and vinyl chloride resins. Studies are included on the epidemiology of industrial and public exposures to the compound and its degradation and combustion products. (This updated bibliography contains 90 abstracts, 8 of which are new entries to the previous edition). (Author abstract)

152 AU - Belanger PL ; Elesh E
AD - Hazard Evaluations and Technical Assistance, Natl. Inst. Occupational Safety and Health, Cincinnati, OH
TI - HAZARD EVALUATION AND TECHNICAL ASSISTANCE. REPORT NO. HE 78-73-612, KENTILE FLOORS, INC., CHICAGO, ILLINOIS.
SI - ICDB/81/87172
SO - Hazard Evaluation and Technical Assistance. Report No. HE 78-73-612, Kentile Floors, Inc., Chicago, Illinois. Available from National Technical Information Service, Springfield, Va,, as PB80-161094, NIOSH-TR-HHE-78-73-612, 26 pp., 1980.
LA - ENG

AB - An environment and medical survey was conducted on June 26 and 27, and August 19 to 22, 1978 at Kentile Floors, Incorporated, Chicago, Illinois at the request of an authorized employee representative to determine the potential exposure of 50 employees to asbestos (1332214), polynuclear aromatic hydrocarbons, vinyl chloride monomer (75014), talc (14807966), alpha methyl styrene (98839), and numerous organic and inorganic dyes and pigments used in the production of vinyl asbestos and asphalt asbestos floor coverings. None of the test chemicals exceeded the OSHA recommended criteria, and no cases of asbestosis or other occupationally related disease were documented among the past or present workers. The investigators recommend that the company review their material inventory for potentially toxic chemicals and periodically monitor these chemicals and that employees be instructed on proper respirator use and other safety precautions. A canopy exhaust system should be installed, carcinogenic chemicals should be identified and stored separately from noncarcinogens, the ventilation exhaust systems should be inspected periodically, and workers potentially exposed to asbestos should change clothes and shower before leaving the workplace. (Author abstract)

153 AU - Anderson D ; Richardson CR ; Waight TM ; Purchase IF ; Adams WG
AD - Central Toxicology Lab., Imperial Chemical Industries Ltd., Alderley Park, Macclesfield, Ches. SK10 4TJ, England
TI - CHROMOSOMAL ANALYSES IN VINYL CHLORIDE EXPOSED WORKERS. RESULTS FROM ANALYSIS 17 AND 42 MONTHS AFTER AN INITIAL SAMPLING.
SI - ICDB/81/86316
SO - Mutat Res; 79(2):151-162 1980
LA - ENG
AB - The second and third blood samplings were taken from workers occupationally exposed to either vinyl chloride or polyvinyl chloride, and the incidences of chromosomal aberrations were compared to the previously reported results of the first sampling. The second and third samplings were taken 18 and 42 mo, respectively, after the first sampling. Threshold limit values for vinyl chloride and plant exposure were reduced after the first sampling. The second sampling showed that there was a tendency toward increased chromosomal abnormalities in the vinyl chloride-exposed workers. Workers who had moved away from polyvinyl chloride production had significant decreases in some types of chromosomal damage, compared to the trend for all workers. In the third sampling there was a tendency toward a decrease in the percentage of cells with chromosomal aberrations of various types, compared to both previous samplings. It was concluded that reduction in exposure to vinyl chloride is accompanied by a reduction in the chromosomal abnormalities to levels indistinguishable from those of controls. (13 Refs)

154 AU - Walsh CT
AD - Dept. Chemistry and Biology, Massachusetts Inst. Technology, Cambridge, MA, 02139
TI - SCOPE AND MECHANISM OF ENZYMATIC MONOOXYGENATION REACTIONS.
SI - ICDB/80/85295
SO - Annu Rep Med Chem; 15:207-216 1980
LA - ENG
AB - The role of the iron-, copper-, flavin-, and pteridine-dependent monooxygenases are discussed. In liver metabolism, and to a lesser extent in lung and intestine, P450 monooxygenases are used as the main apparatus for drug metabolism and detoxification of other xenobiotics by sequences that introduce hydroxyl functionality to increase polarity and so facilitate aqueous solubility and urinary excretion. Exposure of a mammal to a wide variety of xenobiotics (eg, phenobarbital, 3-methylcholanthrene) induces high levels (up to 10% of the protein of liver cell endoplasmic reticulum) of a family of P450 isozymes. The detoxification process, however, occasionally leads to the generation of toxic products. The interaction of P450 with nitrosamines, benzo(a)pyrene, vinyl chloride, or thiocarbamate herbicides can form biologically harmful products. Darvon can titrate out P450 drug metabolism capacity, changing pharmacokinetic disposition of other drugs and generating profound pharmacological alterations. (66 Refs)

155 AU - Thiess AM ; Frentzel-Beyme R ; Link R ; Wild H
AD - Arbeitsmedizin une Gasundheitsschutz, BASF Aktiengesellschaft, 6700 Ludwigshafen, W. Germany
TI - MORTALITY STUDY OF CHEMICAL INDUSTRY WORKERS IN VARIOUS ESTABLISHMENTS WHO WERE ALSO EXPOSED TO ACRYLONITRILE.
SI - ICDB/80/84521
SO - Zentralbl Arbeitsmed Arbeitsschutz Prophyl; 30(7):259-267 1980
LA - GER
AB - A mortality study of 1,469 chemical industry workers exposed to acrylonitrile (AN) and to various other organic substances (including vinyl chloride, ethyl benzol, acrylamide, nitrobenzol, and phenol) is described. There were 89 deaths among these workers employed in 12 West German plants before May 15, 1978. Based on the population of West Germany, 99 deaths would have been expected. Twenty-seven of the observed deaths were due to malignant neoplasms, whereas only 20.7 such deaths would have been expected; the difference is not statistically significant, however. The ratios of observed to expected deaths were 11:5.6 for lung carcinomas and 4:1.7 for neoplasms of the lymph nodes and hematopoietic tissues; these differences are statistically significant. Deaths due to natural causes were equal to or below the expected number, but there were nine suicides (5.2 expected). Because of the multiple exposures, a specific AN-related cancer risk is difficult to estimate. Based on animal experiments and other epidemiological studies, however, there are reasons to suspect that AN is carcinogenic. (13 Refs)

156 AU - Wisniewska-Knypl JM ; Klimczak J ; Kolakowski J
AD - Dept. Biochemistry, Inst. Occupational Medicine, Teresy 8, 90-950 Lodz, Poland
TI - MONOOXYGENASE ACTIVITY AND ULTRASTRUCTURAL CHANGES OF LIVER IN THE COURSE OF CHRONIC EXPOSURE OF RATS TO VINYL CHLORIDE.
SI - ICOB/80/83851
SO - Int Arch Occup Environ Health; 46(3):241-249 1980
LA - ENG
AB - The effect of long-term repeated exposure of Wistar rats to vinyl chloride (VC: 50, 500, and 20,000 ppm) on the activity of cytochrome P-450 monooxygenase (MOA) and the ultrastructure of the liver was investigated. The rats were exposed for 5 hr/day, 5 days/wk for 10 mo. Measurements were performed after 1, 3, 6, and 10 mo of exposure. After 1 and 3 mo of exposure to 500 and 20,000 ppm VC, the level of MOA was slightly lower than in controls, and was restored to the original level upon continued exposure; a slight increase in the activity of aniline p-hydroxylase was noted. The development of liver enlargement was accompanied by ultrastructural alterations beginning in the third mo of exposure at all concentrations. Hepatic alterations included hypertrophy of smooth and rough endoplasmic reticulum, swelling of the mitochondria, accumulation of lipid droplets, and focal cytoplasmic degradation. These changes are discussed with respect to the activity of the MOA system in metabolizing VC to toxic metabolites. (23 Refs)

157 AU - Darnis F
AD - Hospital Saint-Antoine, 75012 Paris, France
TI - ROLE OF DIETARY FACTORS IN THE ORIGIN OF PRIMARY LIVER CANCER.
SI - ICOB/80/82951
SO - Gaz Med Fr; 87(22):2863-2866,2868,2870 1980
LA - FRE
AB - Primary liver cancer is 100 times more frequent in Senegal, northern Mali, Mozambique, and Zimbabwe than in western nations. This unequal distribution is not due to genetic or racial factors, since liver cancer is equally frequent among whites and blacks in the United States. The presence of certain substances in the human environment, especially in foods, helps to explain the disparity. Among the most important of these substances are mycotoxins, including aflatoxin, sterigmatocystine, luteoskyrine, cyclochlorotine; nitrosamines such as diethylnitrosamine, N-nitrosopyrrolidine, ethylnitrosourea, and gluconodeltalactone; and halogenated ethylenes, including vinyl chloride, trichloroethylene, and polyvinyl chloride. Although many of these substances are released into the environment during manufacturing and combustion, there are also many which are natural products and contaminate improperly stored foods (aflatoxin) and drinking water supplies. Because human cancer is of multifactorial origin, the notion of a 'threshold dose' below which consumption is safe may be an illusion. (3 Refs)

158 AU - Krajewski J ; Dobecki M ; Milczarska A
AD - Zaklad Chemicznych Zanieczyszczen, Instytut Medycyny Pracy, ul. Teresy 8, 90-950 Lodz, Poland
TI - EVALUATION OF THE WORKING ENVIRONMENT IN PVC PLANTS.
SI - ICDB/80/82946
SO - Med Pr; 31(2):149-153 1980
LA - POL
AB - The atmospheric concentrations of vinyl chloride (VC) were measured during the first 4 yr of operation of a VC plant in Poland. The highest concentrations (258-1,880 mg/cubic meter) were measured during the cleaning of pressure vessels. It was possible to reduce the VC emissions considerably through technical measures. (7 Refs)

159 AU - Higginson J ; Coe JT ; Lang RA
AD - Lyon, France
TI - REGULATING CARCINOGENS IN THE WORKPLACE (3 LETTERS TO EDITOR).
SI - ICDB/80/80753
SO - Technol Rev; 82(8):2,88 1980
LA - ENG
AB - Comments on Samuel Epstein's article 'Cancer, Inflation, and the Failure to Regulate' (December/January 1980, Technol Rev) are presented. One document cited in the article was incorrectly said to have been prepared by experts from the International Agency for Research on Cancer. Representatives of industry reaffirm their positive contributions to and suggestions for researching and regulating the levels of carcinogens in the workplace. Examples of such carcinogens were acrylonitrile and heavy vinyl chloride. (no Refs)

160 AU - Anderson MW ; Hoel DG ; Kaplan NL
AD - Lab. Pharmacokinetics, Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC, 27709
TI - A GENERAL SCHEME FOR THE INCORPORATION OF PHARMACOKINETICS IN LOW-DOSE RISK ESTIMATION FOR CHEMICAL CARCINOGENESIS: EXAMPLE - VINYL CHLORIDE.
SI - ICDB/80/80030
SO - Toxicol Appl Pharmacol; 55(1):154-161 1980
LA - ENG
AB - It is suggested that the fate of carcinogens is not always dose dependent but that covalent binding to DNA produces the genotoxic effect that is the initiating event of carcinogenesis. A general scheme is proposed for low-dose extrapolation of carcinogenesis, based on the DNA-carcinogen adduct formed. A pharmacokinetic model is presented, relating exposure concentration to the amount of DNA-carcinogen adduct formed. Two pharmacokinetic models for vinyl chloride are presented. (12 Refs)

R&S 139058

161 AU - Pialat J ; Pasquier B ; Pahn M ; Koop N
AD - Lab. d'Anatomie Pathologique, C.H.U. de Lyon, Faculte Alexis Carrell, rue Guillaume-Paradin, 69372 Lyon, France
TI - HEPATIC LESIONS CAUSED BY VINYL CHLORIDE MONOMER (CVM).
SI - ICDB/80/79932
SO - Sem Hop Paris; 56(25-28):1188-1202 1980
LA - FRE
AB - The history of discoveries concerning the carcinogenic character of vinyl chloride monomer (VCM) are reviewed and include the discovery of its mutagenic role, its carcinogenic effect on humans, and its relationship with hepatic fibroses. Case studies are presented for six hepatic angiosarcomas (HA), one malignant hepatoma, and one fibrosis in patients chronically exposed to VCM. All patients were men (av age 51 yr) who worked in industries with VCM for 10-30 yr. Hepatomegaly was a common finding in HA cases, although all other clinical and histological findings were typical. Unlike other cases of hepatoma which have been secondarily reclassified as HA, the case in this series was clearly a hepatoma. The case of fibrosis was classified as isolated fibrosis secondary to VCM. (111 Refs)

162 AU - Hogstedt C ; Westerlund B
AD - Orebro, Sweden
TI - MORTALITY OF FOREST WORKERS EXPOSED AND UNEXPOSED TO PHENOXY ACID PREPARATIONS.
SI - ICDB/80/76947
SO - Lakartidningen; 77(19):1828-1831 1980
LA - SWE
AB - Mortality and tumor incidence of 142 forest workers exposed to phenoxy acid preparations, 244 unexposed workers, and 16 foremen were investigated in an epidemiological study using payrolls from the 1950's and 1960's. The highly exposed foremen showed significantly greater incidence of tumors compared with normal values taken from the cancer registry statistics. Occupational exposure to various phenoxy acid preparations, ie amitrol, 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) and its derivative, TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin), and 2,4-D (2,4-dichlorophenoxyacetic acid) resulted in malignant soft-tissue tumors. These compounds are also teratogenic and mutagenic. Aerial spraying with 2,4,5-T was implicated in miscarriages in Oregon and chromosomal damage in Vietnam. Phenoxy preparations have been used in Sweden since the early 1950's for control of vegetation. The subjects of the study were divided in three groups: exposed workers (more than 5 days exposure), foremen (highest exposed), and unexposed. Many of the 142 exposed workers had also planted DDT-treated trees. The foremen had higher mortality and tumor deaths than normal (3 to 1), while tumor deaths were lower than normal both among exposed and unexposed workers. With minimum 60 days exposure tumor mortality increased and this trend became stronger with 120 days exposure. The higher tumor deaths among the foremen might have been associated with their greater exposure to phenoxy acid

preparations. It is conceivable that phenoxy acid preparations, just like vinyl chloride, increase the incidence of certain types of tumors but that their overall carcinogenicity is relatively low or moderate. (15 Refs)

163 AU - Blejer HP
AD - City of Hope Hosp., City of Hope, CA
TI - IS YOUR PATIENT'S JOB KILLING HIM?
SI - ICDS/80/76430
SO - Med Times; 108(7):91-95 1980
LA - ENG
AB - Occupational carcinogenesis is discussed. The dangers of exposure to anesthetic gases, arsenic, asbestos, benzene, carbon disulfide, carbon tetrachloride, coal, coke oven emission, DBCP, DDT, lead, mercury, talc, vinyl chloride, styrene, butadiene, chromium, bis(chloromethyl)ether, uranium, chloromethyl methyl ether, chromates, nickel, soots and tars, isopropyl oils, wood dusts, cutting oil, 4-aminobiphenyl, benzidine, beta-naphthylamine, magenta, 4-nitrodiphenyl, auramine, chloroprene, cadmium, PCBs, beryllium, trichloroethylene, tetrachloroethylene, heptachlor, dieldrin, chloroform, and aldrin are presented in tabular form. (9 Refs)

164 AU - Filser JG ; Bolt HM
AD - Abteilung fur Toxikoligie, Pharmakologisches Institut der Universitat Mainz, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany
TI - CHARACTERISTICS OF HALOETHYLENE-INDUCED ACETONEMIA IN RATS.
SI - ICDS/80/76255
SO - Arch Toxicol (Berl); 45(2):109-116 1980
LA - ENG
AB - A series of halogenated ethylenes (vinyl chloride, vinylidene fluoride, cis- and trans-1,2-dichloroethylene, perchloroethylene) induces increased acetone exhalation in rats. Exposures of differently pretreated rats to vinylidene fluoride suggest that a metabolite of the haloethylene must be involved in eliciting this formation of acetone. This conclusion is based on (a) dependence of acetone exhalation on the concentration of vinylidene fluoride, (b) effect of inducing agents, (c) effect of pyrazol, a metabolic inhibitor, (d) effect of cysteine, (e) effect of hypoxia and (f) the time course of acetone exhalation. (Author abstract) (11 Refs)

165 AU - Munakata H ; Yosizawa Z
AD - Dept. Biochemistry, Tohoku Univ. Sch. Medicine, 2-1, Seiryo-machi, Sendai 980, Japan
TI - ISOLATION AND CHARACTERIZATION OF A SULFATED GLYCOPROTEIN FROM A TRANSPLANTABLE COLORECTAL ADENOCARCINOMA OF RATS.
SI - ICDS/80/75722
SO - Biochim Biophys Acta; 623(2):412-417 1980
LA - ENG
AB - A transplantable colorectal adenocarcinoma from rats of the ACI/N strain was extracted with 5 milliM EDTA (pH 7.0), and

fractionated by gel filtration on Sepharose 4B, followed by preparative poly(vinyl chloride) zone electrophoresis. An acidic glycoprotein (SGP) thus obtained was shown to be homogeneous by electrophoresis on cellulose acetate membrane and on sodium dodecyl sulfate agarose gel. SGP contained 61.9% carbohydrate, 28.9% total amino acids and 1.4% sulfate. The major monosaccharides in SGP were galactose, glucosamine and galactosamine. Small quantities of sialic acid, L-fucose and mannose were also present. Threonine, serine, proline, glutamic acid and aspartic acid were the major amino acids of the protein moiety. (Author abstract) (13 Refs)

166 AU - Basler A ; Rohrborn G
AD - Institut fur Humangenetik und Anthropologie der Universitat, Universitatsstrasse 1, Gebaude 23.12, D-4000 Dusseldorf 1, W. Germany
TI - VINYL CHLORIDE: AN EXAMPLE FOR EVALUATING MUTAGENIC EFFECTS IN MAMMALS IN VIVO AFTER EXPOSURE TO INHALATION.
SI - ICDS/80/73932
SO - Arch Toxicol (Berl); 45(1):1-7 1980
LA - ENG
AB - As part of a program of investigations on the mutagenic effects in mammals in vivo after inhalation of environmental chemicals, the effect of the industrial compound vinyl chloride (VC) was analyzed. Chinese hamsters were exposed to 1.25%, 2.5% or 5% (v/v) VC in air for 6, 12 or 24 hr. Bone marrow chromosomes were analyzed for induced chromosome aberrations and sister-chromatid-exchanges (SCEs) 26 hr after beginning of exposure. The frequency of VC-induced chromosome aberrations and SCEs both depend on dose and length of exposure. The highest measured effects were 33.25 SCEs/cell after an exposure to 2.5% VC for 24 hr and 25.7% metaphases with aberrations, when exposed to 5% VC for 24 hr. (Author abstract) (21 Refs)

167 AU - Buchter A ; Filser JG ; Peter H ; Bolt HM
AD - Institut und Poliklinik fur Arbeits- und Sozialmedizin, Universitat Koln, Josef-Stelzmann-Strasse 9, D-5000 Koln 41, W. Germany
TI - PHARMACOKINETICS OF VINYL CHLORIDE IN THE RHESUS MONKEY.
SI - ICDS/80/72558
SO - Toxicol Lett; 6(1):33-36 1980
LA - ENG
AB - The pharmacokinetics of vinyl chloride (VC) were assessed in Rhesus monkeys exposed to various air concentrations of VC in a closed system. When the animals were exposed to VC concentrations of up to 200 ppm, VC disappeared from the atmosphere according to a first-order law. The clearance was 3.55 liters/hr/kg body wt, but could be decreased by 90% after administration of the metabolic inhibitor disulfiram. When the absolute rates of VC metabolism were plotted against the VC exposure concentrations, first-order kinetics applied for the 200-300-ppm concentration range. At higher concentrations, the plotted curve was nonlinear and showed saturation characteristics. Based on the first-order

metabolic rates of VC in Rhesus monkeys, it is concluded that this species is a closer approximation to man than other animal models. For example, rats, mice, and gerbils metabolize VC 5-12x faster than humans. (8 Refs)

168 AU - Padgett J
AD - Office Air Quality Planning and Standards, Environmental Protection Agency, Research Triangle Park, NC, 27711
TI - POLICY AND PROCEDURES FOR IDENTIFYING, ASSESSING, AND REGULATING AIRBORNE SUBSTANCES POSING A RISK OF CANCER.
SI - ICDB/80/68184
SO - Fed Regist; 45(106):36987-36989,37116 1980
LA - ENG
AB - The Environmental Protection Agency's proposed policy for controlling emissions of airborne carcinogens (eg, asbestos, vinyl chloride, and benzene) is reviewed. The policy is based on the application of the best available technology. In most cases, the emission standards will be in the form of performance standards. Where applicable, generic standards will be used for the control of fugitive emissions from industrial sources. The benefits of the standards, the sources affected, and related regulations and actions are summarized. (3 Refs)

169 AU - Gingell R ; Brunk G ; Leuschen T ; Gold B
AD - Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, 42 and Dewey Ave., Omaha, NE, 68105
TI - EVIDENCE FOR METABOLIC EPOXIDATION OF A DDT METABOLITE (MEETING ABSTRACT).
SI - ICDB/80/62158
SO - Proc Am Assoc Cancer Res; 21:112 1980
LA - ENG
AB - 1,1,1-trichloro-2-bis(p-chlorophenyl)ethane (DDT) is metabolized via the series of intermediates DDD, DDNU, DDNS, DDNU and DDOH to DDA (structures are given) which is excreted in the urine free and as conjugates. DDNU is a chloroolefin analogous to vinyl chloride which is metabolically activated to a carcinogen by epoxidation. We have performed studies to determine if DDNU is also metabolized via a chloroepoxide which would be highly reactive and might account for the carcinogenicity of DDT and DDD in mice. Rearrangement of the hypothetical chloroepoxide would yield metabolites which could be further oxidized and excreted as either or both alphahydroxy-DDA (OH-DDA) or alphachloro-DDA (Cl-DDA). OH-DDA has been detected in the urine of mice given 500 mg/kg po DDNU (approx 1% dose), together with DDOH and DDA, whereas after administration of DDNS, the next metabolic intermediate, only traces (less than 0.05%) were recovered as OH-DDA. These results suggest that DDT is metabolized in vivo to some extent via a reactive chloroepoxide which might be an ultimate carcinogenic metabolite. (no Refs)

170 AU - Kraybill HF
AD - NCI, Room 3C37, Landow Building, Bethesda, MD, 20205
TI - EVALUATION OF PUBLIC HEALTH ASPECTS OF CARCINOGENIC/MUTAGENIC BIOREFRACTORIES IN DRINKING WATER.
SI - ICDB/80/61845
SO - Prev Med; 9(2):212-218 1980
LA - ENG
AB - Environmental Protection Agency monitoring systems have identified 699 biorefractories in United States water supplies. From an original list of 309 biorefractories in 1977, the NCI has identified and classified 23 carcinogens, 30 mutagens, and 11 promoters in drinking water. The carcinogens include: benzo(a)pyrene, carbon tetrachloride, chloroform, vinyl chloride, 1,4-dioxane, methyl iodide, DDE, DDT, chlordane, lindane, dieldrin, benzene, vinylidene chloride, heptachlor, 1,1,2-trichloroethane, 1,1,2-trichloroethylene, bis(2-chloroethyl)ether, simazine, tetrachloroethylene, heptachlor epoxide, acrylonitrile, aldrin, and butyl bromide. The results of 12 reported epidemiologic studies on drinking water indicate that the risk of cancer may be greater in the following situations: surface water greater than ground water, chlorinated water greater than nonchlorinated water, high levels of trihalomethanes (THM) greater than low levels of THM, and water from highly polluted surface water such as the Mississippi greater than surface water from less polluted waters. These studies have also suggested some association between THM and an increased frequency of bladder cancer. However, the results do not establish causality, and estimates of increased or decreased risk are extremely crude since effects of other factors, such as cigarette smoking, have not been ascertained. (16 Refs)

171 AU - Upton AC
AD - Dept. Environmental Medicine, New York Univ. Medical Center, New York, NY
TI - FUTURE DIRECTIONS IN CANCER PREVENTION.
SI - ICDB/80/61195
SO - Prev Med; 9(2):309-314 1980
LA - ENG
AB - The detection and characterization of risk factors is discussed in relation to designing future programs of cancer prevention. Such risk factors include various lifestyle factors (eg, UV radiation exposure, tobacco, and alcohol), dietary factors (eg, aflatoxin, safrole, and bracken fern), drugs (eg, diethylstilbestrol and chlornaphazine), and occupational factors (eg, ionizing radiation, vinyl chloride, and asbestos). Also relevant are various preneoplastic conditions predisposing to the development of cancer such as familial polyposis of the colon, xeroderma pigmentosum, Down's disease, Fanconi's anemia, atrophic gastritis, and leukoplakia. The success of future cancer prevention programs is discussed in terms of the integration of a broad range of disciplines, intensified efforts at professional and public education, and close coordination with allied health

and regulatory agencies. (20 Refs)

172 AU - Tompa A
AD - Kiserleti Patologiai Osztaly, Orszagos Munka es Uzemegeszsegugyi Intezet, Budapest, Hungary
TI - METHODS FOR THE IN VITRO STUDY OF THE EFFECTS OF CARCINOGENIC SUBSTANCES.
SI - ICDB/80/60982
SO - Orv Hetil; 121(7):555-561 1980
LA - HUN
AB - Methods for the in vitro study of the effects of carcinogenic substances are discussed with special regard to the Ames test. Substances found to be carcinogenic in humans include aflatoxins, 4-aminobiphenyl, asbestos, arsenic compounds, auramine, benzene, bis-chloromethyl ether, benzidine, cadmium oxide, chloramphenicol, chloromethyl ether, chromium compounds, cyclophosphamide, diethylstilbestrol, isopropyl oil, melphalan, mustard gas, 2-naphthylamine, nickel compounds, N,N-bis-(2-chloroethyl)-2-naphthylamine, oxymethalone, fenitoine, soot, tar, and vinyl chloride. The Ames test can give false-positive and false-negative results for some compounds; eg, such non-carcinogenic substances as 4-acetylaminofluorene, alpha-naphthylamine, Folpet P, benzo(a,e)pyrenes, dibenzo(a,h)-anthracene, glycidol, 1,2-epoxybutane, 5-nitro-2-furamidoxime, 1[(-nitrofurylidene)-amino] hydantoine, 5-nitro-2-furacilic acid, sodium nitrite, and sodium azide were found to be mutagenic in the Ames test. On the other hand, such carcinogens as O-toluidine, auramine, carbon tetrachloride, chloroprene, dieldrin, thiourea, urethane, thioacetamide, acetamide, ethionine, saffrol, 1-hydroxy-saffrol, cicasine, sodium phenobarbital, 4-aminoantipyrene, amitrol, and 1,2-dimethylhydrazine, are non-mutagenic in the Ames' test. (48 Refs)

173 AU - Rawls R
AD - No affiliation given
TI - STUDIES UPDATE VINYL CHLORIDE HAZARDS.
SI - ICDB/80/60010
SO - Chem Eng News; 58(14):27-28 1980
LA - ENG
AB - Various animal and epidemiological studies presented at a NIH conference on vinyl chloride (VC) and its possible hazards were summarized in this brief report. Cesare Maltoni of the Istituto de Oncologia in Bologna, Italy, examined the effects of VC and a few structurally similar compounds in mice, hamsters, and rats for a total of 3 million rodent days and concluded that VC was a multipotent carcinogen in rodents. Liver angiosarcomas and other tumors were found in animals treated by inhalation with as little as 10 ppm VC or ingestion of 0.3 mg VC/Kg body wt. Peter Infante, Occupational Safety and Health Administration, summarized various human epidemiological studies which, taken together, indicated a greater incidence of brain cancers than of liver cancers among workers exposed to VC. Tabershaw-Cooper Associates conducted for

the Chemical Manufacturer's Association an extensive epidemiological study of 10,173 workers in 37 of 43 plants producing VC or polyvinyl chloride (PVC). Workers with high VC exposure did not die earlier than in the control population nor were they more likely to die from cancer; however, cancers of the brain, CNS, digestive system and respiratory system were more common in the VC workers. In several other studies it was shown that PVC particles could be picked up by the lungs of animals or man. Exposure to PVC dust caused some changes in lung x-rays and in lung functions. VC was shown to cause mutations in bacteria. The question of whether VC might pose a reproductive hazard was not conclusively answered. (no Refs)

174 AU - Dalri P
AD - Divisione di Medicine Generale I, Ente Ospedaliero Generale Regionale 'S. Chiara', Trento, Italy
TI - EPIDEMIOLOGY OF LUNG TUMORS.
SI - ICDB/80/60007
SO - Minerva Med; 71(4):265-268 1980
LA - ITA
AB - Epidemiological data on lung cancer are presented. The incidence of lung cancer has been growing, especially in women, due to the increasing percentage of smoking women. The lung cancer mortality in the United States white population was 1.55/100,000 in men and 1.50/100,000 in women in 1923, vs 63.20/100,000 in men and 12.40/100,000 in women in 1969. The carcinogenic factors include radioisotopes, 3,4-benzopyrene, 3,4,9,10-dibenzopyrene, asbestos (which causes bronchogenic carcinoma and mesothelioma), haloethers, nickel chromates, inorganic arsenic, hematite, vinyl chloride, and printing ink. Diseases involving immune disorders or immunodepression (scleroderma, sarcoidosis, pneumoconiosis) can predispose to lung cancer, which is manifested in increased lung cancer incidence among such patients. (6 Refs)

175 AU - Zuccato E ; Marcucci F ; Mussini E
AD - Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milan, Italy
TI - THE ROLE OF RESPIRATION IN VINYL CHLORIDE MONOMER EXCRETION IN RATS.
SI - ICDB/80/58718
SO - Toxicol Lett; 5(3/4):213-217 1980
LA - ENG
AB - The effect of respiratory activity on the kinetics of pulmonary excretion of vinyl chloride monomer (VCM) was studied. In the first experiment, VCM was injected (1, 5, or 10 mg/kg aqueous soln, iv) into a femoral cannula of anesthetized male CD-COBS rats that were breathing through a tracheal cannula connected to a pump operating at a fixed flow rate of 30 ml/min (22 respirations/min). At 1-min intervals after the VCM injection, expired air and blood samples were collected and analyzed for VCM. It was found that VCM concentrations in the expired air and blood were proportional to the amount injected; VCM disappearance curves from the lungs and blood appeared to be linear at 1 mg/kg,

and biphasic at 5 and 10 mg/kg. In a second experiment, VCM was injected (5 mg/kg, iv) while the pump flow rates (pulmonary ventilation) were set at 14, 30, or 70 ml/min. The results showed that the VCM excretion rate was directly proportional to pulmonary ventilation. No significant difference was noted between VCM blood levels in the various conditions. In a third experiment, in which respiration was stopped for 1 min and then continued at a flow of 30 ml/min, there was no decrease in blood VCM levels while respiration was stopped. The blood VCM levels of rats with respiratory-stop and rats with normal respiration were significantly different. The results of these experiments showed that VCM is mainly eliminated through the lungs. Over 90% of the VCM was exhaled in rat breath in 4 min after an iv VCM injection. (5 Refs)

176 AU - Doss M
AD - Abteilung fur Klinische Biochemie, Fachbereich Humanmedizin der Philipps-Universitat, Pilgrimstein 2, D-3550 Marburg an der Lahn, W. Germany
TI - PATHOBIOCHEMICAL TRANSITION OF SECONDARY COPROPORPHYRINURIA TO CHRONIC HEPATIC PORPHYRIA IN HUMANS.
SI - ICDB/80/58098
SO - Klin Wochenschr; 58(3):141-148 1980
LA - ENG
AB - Secondary coproporphyrinurias can be observed in one third of all patients affected by liver damage, especially by alcohol liver syndromes. Potentially, every secondary coproporphyrinuria can turn into a chronic hepatic porphyria, which progresses along several biochemically detectable latent phases and which indicates clinical manifestation by cutaneous symptoms. Two requirements are necessary for the transition of a secondary coproporphyrinuria to a chronic hepatic porphyria: 1) Genetic disposition of an autosomal dominantly inherited defect in uroporphyrinogen decarboxylase, which only becomes subclinically or clinically relevant through alcohol or estrogens (also oral contraceptives) in connection with liver damage; 2) A toxic inhibition of uroporphyrinogen decarboxylase in the liver caused by polyhalogenated hydrocarbons, such as hexachlorobenzene, polychlorinated and polybrominated biphenyls, dioxins and probably also methyl and vinyl chloride in combination with a present liver damage or caused by one of these agents. Experimental results, further, prove a direct negative effect of alcohol on the activity of uroporphyrinogen decarboxylase. In all liver conditions one should look out for porphyrinuria, because it represents an important criterion for toxic liver damage and early diagnosis of a chronic hepatic porphyria is assessed by differentiating hepatic porphyrinurias. (Author abstract) (27 Refs)

177 AU - Boorman GA ; McConnell EE ; Cockrell BY ; Drew RT ; Stone GA
AU - Haseman JK ; Moore JA
AD - NIH, Natl. Inst. Environmental Health Science, Resarch Triangle Park, NC, 27709
TI - THE COMPARATIVE EFFECTS OF AN ANIMALS AGE AT THE TIME OF EXPOSURE AND EXPOSURE DURATION ON VINYL CHLORIDE CARCINOGENESIS (MEETING ABSTRACT).
SI - ICDB/80/55151
SO - Fed Proc; (3,part1):546 1980
LA - ENG
AB - Vinyl chloride was used as a model compound to determine the effect of exposure duration and age of animal at time of exposure on tumor induction. Groups of 56 Golden Syrian hamsters, F344 rat, Swiss mice and B6C3F1 mice were exposed to 200 ppm or 100 ppm of vinyl chloride, respectively, for 6 hr a day, 5 days a wk according to the following regimens; 0-6, 0-12, 0-18, 0-24, 6-12, 6-18, 12-18, 12-24 and 18-24 mo and were compared to unexposed controls. Following exposure all animals were held until found moribund or dead at which time a complete necropsy examination was performed. Histopathological examination of hamsters revealed the following exposure related tumors: hemangiosarcomas (primary tumor usually in the skin), tumors of the nonglandular stomach and mammary tumors. In the rats, exposure related tumors included hemangiosarcomas (primary tumor usually in the liver), hepatocellular tumors and mammary tumors). Early exposure (0-6 mo following weaning) resulted in a similar tumor incidence as continuous exposure (0-24 mo following weaning) and 6 mo exposure early in life resulted in a higher tumor incidence when compared to animals exposed for a similar time period later in life. (no Refs)

178 AU - de Meester C ; Duverger-van Bogaert M ; Lambotte-Vanderpaer M
AU - Roberfroid M ; Poncelet F ; Marcier M
AD - Lab. Biotioxicology, Univ. Louvain, Sch. Pharmacy, U.C.L.-73.69, B. 1200 Brussels, Belgium
TI - MUTAGENICITY OF VINYL CHLORIDE IN THE AMES TEST. POSSIBLE ARTIFACTS RELATED TO EXPERIMENTAL CONDITIONS.
SI - ICDB/80/54412
SO - Mutat Res; 77(2):175-179 1980
LA - ENG
AB - To demonstrate that variations in experimental conditions used to evaluate the mutagenicity of vinyl chloride monomer (VCM) in the Ames test could explain some discrepancies observed between previously reported results, four series of experiments were carried out under different conditions. The results showed that VCM exerted direct mutagenic activity toward Salmonella typhimurium TA1530, and this was related to VCM concentration in the atmosphere. The mutagenicity of VCM was strongly enhanced in the presence of S9 mix. However, the mutation frequency for the bacteria was enhanced when plates containing either bacteria alone or S9 alone were co-incubated in an atmosphere of VCM; the mutation frequency was not enhanced when plates containing

bacteria alone were incubated in an atmosphere of VCM, without the co-incubation of plates containing S9 alone. The increase in mutation frequency was more pronounced when the S9 mix was derived from Aroclor-treated mice. These results suggest that the observed enhancement of VCM mutagenicity is correlated with the formation, under the influence of S9 liver-metabolizing enzymes, of mutagens such as the volatile intermediate compounds chloroethylene oxide and 2-chloracetaldehyde. Quantitative results could be affected by numerous experimental conditions; the quantity of volatile metabolites, the vol of the experimental chamber, the number of plates, and the composition of the plates. (6 Refs)

179 AU - Koller LD
AD - Veterinary Medicine, Univ. Idaho, Moscow, ID, 83843
TI - PUBLIC HEALTH RISKS OF ENVIRONMENTAL CONTAMINANTS: HEAVY METALS AND INDUSTRIAL CHEMICALS.
SI - ICOB/80/53793
SO - J Am Vet Med Assoc; 176(6):525-529 1980
LA - ENG
AB - Hazards to human health which are presented by the heavy metals and by the industrial compounds lead, cadmium, methylmercury, polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), chemical carcinogens, asbestos, and vinyl chloride are reviewed. Humans are exposed to lead from lead-base paints, dust and dirt, ambient air (burning of coal and leaded gasoline), and industry (lead ore smelter, data reproduction, ceramics, newsprint, plastics and illegally distilled liquor), affecting the nervous system and kidneys. Cadmium is found in water, meats, grains, dairy products, pigments, plastics, stabilizers, alloys, batteries, cigarette smoke, and electroplating materials, causing an iron-deficient, microcytic hypochromic anemia and reduced concentrations of Hb. Methylmercury is found in chloroalkali plants, industrial processes, paper-pulp industry limacides, fossil fuels, and other sources, causing cerebral palsey-like disease in infants and loss of sensation and death in adults. PCBs are found in electrical capacitors and transformers, heat transfer systems, plasticizer applications, hydraulic lubricants, and other sources, causing mild anemia and hypoproteinemia. A specific case of exposure of animals and humans to PBBs is described including a listing of numerous clinical signs and symptoms. Chemical carcinogenesis is briefly considered. Asbestos is found in such sources as mining and manufacture of insulation, fire resistant materials, paper, plastic, brake linings, acoustic tiles, filters, abrasives and lubricants with inhalation causing collagenous plaques and thickening and adhesions of the pleura. Exposure to vinyl chloride results primarily from the release of gaseous vinyl chloride during its polymerization to polyvinyl chloride and causes angiosarcoma of the liver. (76 Refs)

180 AU - Suzuki Y
AD - Environmental Sciences Lab., Dept. Community Medicine, Mount Sinai Sch. Medicine City Univ. New York, One Gustave Levy Place, New York, NY, 10029
TI - NONNEOPLASTIC EFFECTS OF VINYL CHLORIDE IN MOUSE LUNG.
SI - ICDB/80/52886
SO - Environ Res; 21(1):235-253 1980
LA - ENG
AB - In a previous study, a high incidence of pulmonary tumors (alveologenic neoplasia in mouse lung exposed to vinyl chloride at heavy dose (2,500 and 6,000 ppm) for long durations (5 and 6 mo)) was reported. In the present study, nonneoplastic effects in mouse lung were investigated by light and electron microscopy. As major light microscopic alterations, proliferation and hypertrophy of the terminal bronchiolar cells, consisting of ciliated and Clara cells, hypersecretion of the epithelial mucin in the goblet cells of both the bronchial and the proximal bronchiolar epithelium, hyperplasia of alveolar epithelium, mobilization of alveolar macrophages, and occasional presence of peribronchial of bronchiolar chronic inflammation, were observed. Electron microscopically, Clara cells of the terminal bronchiolar epithelium showed proliferation of the rough and smooth surfaced endoplasmic reticulum and appearance of large and abnormally shaped mitochondria. Similar alterations were found in the ciliated cells. Submicroscopic changes of pulmonary alveoli were represented by focal thickening of the basement membrane, multiple foci of hyperplastic type II cell (the precondition of the alveologenic tumor), active discharge of osmiophilic lamellar bodies from the type II cell and phagocytosis of the bodies by macrophages, appearance of cholesterol crystalloids in the macrophages, degeneration of alveolar septal cells and occasional appearance of a large nucleus with swelling of the capillary endothelium. (Author abstract) (32 Refs)

181 AU - Peter S ; Ungvary G
AD - Lab. Human Genetics, State Inst. Hygiene, Budapest, Hungary
TI - LACK OF MUTAGENIC EFFECT OF VINYL CHLORIDE MONOMER IN THE MAMMALIAN SPOT TEST.
SI - ICDB/80/52812
SO - Mutat Res; 77(2):193-196 1980
LA - ENG
AB - A mammalian spot test was used to determine whether vinyl chloride monomer (VCM) is able to induce somatic gene mutations. C57BL/6J Han female mice (a/a; wild-type) were mated to the Han rotated-bred males of the T-stock strain (a/a, non-agouti; b/b, brown; cchp/cchp, chinchilla, and pinked eye dilution; dse/dse, dilute and short ear; s/s, piebald spotting). Ten days later, the females were exposed to VCM (12,000 mg/meter3; 4,600 ppm) for 5 hr. F1 offspring were examined at 3-5 wk postpartum for the appearance of mosaic coat colors. As a positive control, the ability of cyclophosphamide (CP: 10 mg/kg) to induce colored spots in F1 hybrids was examined. There was no difference in av

litter size at birth or at 3-5 wk after birth for the VCM, CP, or control groups. No offspring of the VCM-treated group had abnormal morphology; mid-ventral white spots appeared at a frequency of 2.8%, not significantly different from controls. In the CP group, there were significant differences in the number of white and colored spots. The colored spots were brownish and distributed randomly among litters. Toxicity studies showed that the dose of VCM was just tolerable, but not yet toxic for the mice. These results provide no evidence that VCM induces somatic gene mutations. (33 Refs)

182 AU - Bingham E
AD - Occupational Safety and Health Admin., Dept. Labor, 200 Constitution Ave., Room N3718, Washington, DC, 20201
TI - OCCUPATIONAL EXPOSURE TO VINYL CHLORIDE AND POLYVINYL CHLORIDE.
SI - ICDB/80/49699
SO - Fed Regist; 45(20):6668-6669 1980
LA - ENG
AB - The time period for submission of written comments in response to a request for information on vinyl chloride and polyvinyl chloride is extended until May 9, 1980. (no Refs)

183 AU - Laib RJ ; Bolt HM
AD - Institut fur Toxikologie, Universitat Tubingen, Wilhelmstrasse 56, D-7400 Tubingen 1, W. Germany
TI - TRANS-MEMBRANE ALKYLATION: A NEW METHOD FOR STUDYING IRREVERSIBLE BINDING OF REACTIVE METABOLITES TO NUCLEIC ACIDS.
SI - ICDB/80/49072
SO - Biochem Pharmacol; 29(3):449-452 1980
LA - ENG
AB - A new method for alkylation of nucleic acids in rat liver microsomal systems by metabolites of xenobiotics is described and compared to a conventional method. Microsomes for both methods were prepared from livers of male Wistar rats; microsomal preparations were incubated with an NADPH-reganerating system under an atmosphere containing vinyl chloride (VC). In the conventional method (A), polyadenylic acid (poly A; 2 mg/ml) was added directly to microsomal preparations; incubation preceded at 37 C for 45 min. In the trans-membrane method (B), microsomal biotransformation and the binding reaction were separated into two compartments by polyamide molecular sieves. The nucleic acid soln, containing 2 mg poly A/ml, was placed in capillary membrane fascicles. The membrane's skeleton was 200 microns thick and the active separation membrane was 0.5 microns thick. The fascicles were bent around a perforated plastic ring and placed in an Erlenmeyer flask; the microsomal incubation mixture surrounded the fascicles. The system was incubated at 37 C for 45 min under an atmosphere containing VC. In both methods, the remaining poly A mixture was dialyzed, lyophilized, and hydrolyzed; the resultant nucleosides were separated by chromatography. Both methods led to the formation of 1,N(6)-ethenoadenosine (EA) moieties in poly A; EA was the major product. Method B produced 10% less EA than method A. The advantage of method B was that it

eliminated problems of recovery of the alkylated nucleic acid after incubation. With method A, only 45.6 +-5.7% poly A was recovered; with method B, 86.0 +-1.7% poly A was recovered. (10 Refs)

184 AU - Zajdela F ; Croisy A ; Barbin A ; Malaveille C ; Tomatis L
AU - Bartsch H
AD - Unit Chemical Carcinogenesis, International Agency Res. Cancer, 150 cours Albert-Thomas, 69372 Lyon Cedex 2, France
TI - CARCINOGENICITY OF CHLOROETHYLENE OXIDE, AN ULTIMATE REACTIVE METABOLITE OF VINYL CHLORIDE, AND BIS(CHLOROMETHYL)ETHER AFTER SUBCUTANEOUS ADMINISTRATION AND IN INITIATION-PROMOTION EXPERIMENTS IN MICE.
SI - ICDB/80/45621
SO - Cancer Res; 40(2):352-356 1980
LA - ENG
AB - Repeated sc administration of chloroethylene oxide, a reactive metabolite of the carcinogen vinyl chloride, induced local tumors in mice, with an incidence comparable to that of bis(chloromethyl)ether, a structurally related human and animal carcinogen, when both compounds were applied at max tolerated chronically toxic doses; no tumors distant from the injection site were produced. Bis(chloromethyl)ether, chloroethylene oxide, and its rearrangement product chloroacetaldehyde, a highly toxic compound, were further tested in an initiation-promotion experiment. Application to the skin of a single dose of either bis(chloromethyl)ether or chloroethylene oxide, followed by 3 x wkly applications of 12-O-n-tetradecanoylphorbol-13-acetate for 42 wk, produced skin tumors in mice; chloroacetaldehyde under comparable conditions produced no increase in benign or malignant tumors. A good correlation between the chemical reactivity, on the basis of hydrolysis constants in aqueous media, and the carcinogenicity of the three compounds was noted. Our results support the hypothesis that epoxidation of the ethylenic double bond in vinyl chloride yields an ultimate carcinogenic metabolite, chloroethylene oxide, a highly reactive compound which appears also to be largely responsible for the known genetic changes caused by the parent compound. (Author abstract) (36 Refs)

185 AU - Sabadie N ; Malaveille C ; Camus AM ; Bartsch H
AD - Unit Chemical Carcinogenesis, International Agency for Res. on Cancer, 69372 Lyon Cedex 2, France
TI - COMPARISON OF THE HYDROXYLATION OF BENZO(A)PYRENE WITH THE METABOLISM OF VINYL CHLORIDE, N-NITROSOMORPHOLINE, AND N-NITROSO-N'-METHYLPIPERAZINE TO MUTAGENS BY HUMAN AND RAT LIVER MICROSOMAL FRACTIONS.
SI - ICDB/80/42202
SO - Cancer Res; 40(1):119-126 1980
LA - ENG
AB - Carcinogen metabolism in vitro was studied in 20 surgical liver specimens from adult male and female human subjects. A 60-fold interindividual variation in aryl hydrocarbon hydroxylase

(benzo(a)pyrene hydroxylase) activity was seen; the capacity to convert vinyl chloride, N-nitroso-N'-methylpiperazine, and N-nitrosomorpholine into electrophiles mutagenic to Salmonella typhimurium varied 9-, 17-, and 35-fold, respectively. The mean enzymic capacity relative to that of liver from untreated rats was 84% for vinyl chloride, 42% for N-nitrosomorpholine, and 380% for N-nitroso-N'-methylpiperazine. When aryl hydrocarbon (benzo(a)pyrene) hydroxylase activity in human liver specimens was plotted against mutagenicity in S typhimurium mediated by liver microsomes from the same specimens, a positive correlation was obtained in the presence of vinyl chloride (r = 0.55; p less than 0.1), N-nitrosomorpholine (r = 0.86; p less than 0.01), or N-nitroso-N'-methylpiperazine (r = 0.94; p less than 0.01). The results are discussed in relation to the possible development of methods for assessing rates of metabolism of environmental carcinogens in human subjects in vivo using nontoxic drugs that are metabolized by the same enzymes that metabolize carcinogens. Hepatic aryl hydrocarbon (benzo(a)pyrene) hydroxylase activity following treatment of rats with phenobarbitone, pregnenolone-16alpha-carbonitrile, dibenamine, aminoacetonitrile, or disulfiram, but not after treatment with 3-methylcholanthrene, showed a positive correlation with the mutagenicity of the respective 9,000 x gravity liver supernatant fraction mediated in the presence of N-nitrosomorpholine, vinyl chloride, or aflatoxin B1. These data lend further support that cytochrome P-450-linked monooxygenases in rat liver convert N-nitrosomorpholine, vinyl chloride, and aflatoxin B1 into mutagenic electrophiles. (Author abstract) (53 Refs)

186 AU - Maselson MS
AO - Harvard Univ., Cambridge, MA
TI - CHEMICALS AND CANCER.
SI - ICOB/81/10205
SO - Chemicals and Cancer. Boulder, CO, Colorado Associated University Press, 23 pp., 1979.
LA - ENG
AB - Various evidences for the environmental etiology of cancer are reviewed with special attention to identification of environmental carcinogens. In addition to cigarette smoking which was proved to be the principal cause of lung cancer, several other carcinogens were found to cause an elevated risk of cancer of the liver (vinyl chloride, aflatoxin B1), bladder (4-aminobiphenyl, benzidine, chlornaphazine, 2-naphthylamine), skin (arsenic, UV light), lung (asbestos, bis(chloromethyl)ether, mustard gas), vagina (diethylstilbestrol), and corpus uteri (estrogens). High energy radiation was found to induce various types of cancer, and benzene was found to induce leukemia. For most of common types of cancer, the incidence increases with increasing age. Depending on the type of cancer, the incidence increases as the power of age, the power generally ranging between 4 and 6. These findings are consistent with the multistep mechanism of carcinogenesis. Experimental studies indicate that the duration of exposure rather than the chronological age is the

effective time factor in the carcinogenesis. Thus, even if exposure of a population to a carcinogen for one decade induces an extremely low cancer rate, the rates after several more decades can increase significantly. Numerous chemicals induce tumors in experimental animals without interaction with so-called promoters. Nearly all of these carcinogenic chemicals also induce mutations in certain bacteria species. The accuracy of short term tests for carcinogenicity ranges from 86% to 97%. It is emphasized that short term tests and epidemiological studies may be used to identify carcinogens responsible for some of the common cancers. (26 Refs)

187 AU - Stern R
AD - Dept. Pathology, Univ. California, San Fransisco, CA
TI - EXPERIMENTAL ASPECTS OF HEPATIC FIBROSIS.
SI - ICDB/81/93797
SO - Prog Liver Dis; 6:173-185 1979
LA - ENG
AB - A new conceptual framework and model systems to aid in stimulating research in hepatic fibrosis were reviewed. It was concluded that in the study of human fibrosis, the only relevant model appears to be the human. The human has a more vigorous fibrotic response to injury than any other organism. Also, the angiosarcoma that develops in humans after vinyl chloride exposure is accompanied by vigorous fibrosis. Thus tissue culture systems to grow human liver cells take on increased importance in attempts to recreate the fibrous response in vitro. One exploitable model of hepatic fibrosis is the scirrhous response to metastatic tumor. Malignant epithelial cells in the liver induce a dense fibrous response. It has not yet been established if collagen is elaborated by the tumors. (74 Refs)

188 AU - Efthymiou ML
AD - Service du Pr Fournier, Hopital Fernand-Widal, 200, rue du Faubourg Saint-Denis, 75475 Paris Cedex 10, France
TI - HEPATOTOXIC INDUSTRIAL SOLVENTS.
SI - ICDB/81/91806
SO - Med Chir Dig; 8(5):381-382 1979
LA - FRE
AB - Solvents and other hepatotoxic industrial substances are reviewed. The toxic effects of these substances can be manifested in hepatitis, cirrhosis, granulomatosis, steatosis, enzyme induction and inhibition, and hepatic cancer. The carcinogenic hepatotoxic industrial substances include vinyl chloride, nitrosamines, trinitrophenylmethyl nitrosamine, tannins, dimethylaminoazobenzene, As, Se, and Th. (2 Refs)

189 AU - Conso F
AD - Centre Anti-Poisons de Paris, Hopital Fernand-Widal, 200 Fg St-Denis, 75010 Paris, France
TI - HEPATOTOXICITY OF CHLORIDE SOLVENTS DERIVED FROM ALIPHATIC HYDROCARBONS AND OF VINYL CHLORIDE.
SI - ICDB/81/91802
SO - Med Chir Dig; 8(5):431-433 1979
LA - FRE
AB - The hepatotoxicity of aliphatic chloride derivatives varies. The hepatotoxicity is related to the metabolic transformation of the compounds into electrophilic intermediates capable of binding covalently to nucleophilic substances, such as glutathione, and structural and nuclear proteins. Inhalation of carbon tetrachloride, chloroform, 1,2-dichloroethane, tetrachloroethane, and 1,2-dichloropropane has been related to the development of acute hepatitis. Repeated administration of the these solvents has been related to the production of hepatomas in animals. Trichloroethylene seems to have a low level of hepatotoxicity, but has been shown to produce hepatomas in mice. Evidence of the carcinogenicity of vinyl chloride in humans was presented soon after its carcinogenicity in animals was proven. Liver fibrosis with splenomegaly and signs of hypertension, and liver angiosarcoma resulting from exposure to vinyl chloride have been reported. The carcinogenicity of vinyl chloride has been related to its epoxy derivative. Means of detecting the liver toxicity of these solvents are described. (11 Refs)

190 AU - Buffler PA
AD - Univ. Texas Medical Branch, Dept. Preventive Medicine and Community Health, Galveston, TX, 77550
TI - SOME PROBLEMS INVOLVED IN RECOGNIZING TERATOGENS USED IN INDUSTRY.
SI - ICDB/80/79985
SO - Epidemiologic Methods for Detection of Teratogens. Klingsberg MA, Weatherall JA, ed. Basel, S. Karger, Contributions to Epidemiology and Biostatistics, Vol. 1, 203 pp., 1979.
LA - ENG
AB - The possible teratogenicity of vinyl chloride, controversies regarding evidence of vinyl chloride-induced congenital defects, methods used for surveillance of pregnancy outcomes, rationale and methods for an ongoing study of pregnancy outcomes of wives of individuals occupationally exposed to vinyl chloride, and problems encountered in this study are each discussed. The ongoing study includes 248 employees exposed to vinyl chloride and 202 employees who were not exposed. Data on pregnancy outcomes were collected via a standardized telephone interview with the wives of these employees. Various difficulties were encountered in the study. For example, employees were seldom exposed only to vinyl chloride and to no other chemical agent, and other types of exposure (eg, smoking, drinking, drugs) might have an influence on pregnancy outcome. Also, the study group is relatively small, and the reliability of recall of pregnancy outcome probably varies from individual to individual. Additional

research of a methodologic nature is needed to assess the validity and reliability of responses obtained in surveys of this type. (36 Refs)

191 AU - Coulston F ; Lijinsky W ; Martin JH ; Wynder EL ; Frawley JP
AU - Furman RH ; Blair EH ; Harrison Y
AD - Inst. Comparative and Human Toxicology, Albany Medical Coll. of Union Univ., Albany, NY
TI - GENERAL DISCUSSION: THE DELANEY CLAUSE.
SI - ICDB/80/75310
SO - Regulatory Aspects of Carcinogenesis and Food Additives. Coulston F, ed. London, Academic Press, Ecotoxicology and Environmental Quality Series, Vol. 2, 397 pp., 1979.
LA - ENG
AB - Proceedings of a discussion of chemical and environmental carcinogens, extrapolation of experimental data concerning carcinogenesis to humans, and the developement of government policies regulating carcinogen exposure are presented. Studies and epidemiologic data concerned with the carcinogenicity of vinyl chloride, diethylstilbestrol, and saccharin are examined. Current methods of testing of carcinogens are critically evaluated. The percentage of cancers caused by chemicals and by environmental agents is debated, and the applicability of the max tolerated dose bioassay is discussed. The following four steps to be taken in any regulatory policy are outlined: 1) determination of carcinogenicity, 2) determination of the potency of the carcinogen, 3) determination of the actual risk of the exposed population, and 4) comparison of the estimated risk with the estimated benefit. (no Refs)

192 AU - Maekawa A ; Ogiu T ; Odashima N
AD - Div. Pathology, Natl. Inst. Hygienic Sciences, Setagaya-ku, Tokyo 158, Japan
TI - CARCINOGENICITY TEST OF HIGH MOLECULAR COMPOUNDS USED IN MEDICAL PRACTICE BY IMPLANTATION INTO THE SUBCUTANEOUS TISSUE OF RATS (MEETING ABSTRACT).
SI - ICDB/80/67974
SO - Proceedings of the 38th Annual Meeting of the Japanese Cancer Association held in Tokyo, Japan, September 1979. Japanese Cancer Association, Tokyo, Japan, 321 pp., 1979.
LA - JPN
AB - Eleven-wk-old Wistar rats were divided into 4 groups, each consisting of 25 male and 25 female rats. High molecular compounds used in medical practice (vinyl chloride-A for group I, vinyl chloride-B for group II, vinyl chloride-C for group III, and hydrophobic polymer, silicone, for group IV) were cut into plates 1-2 mm thick and 1-2 cm square and implanted into the sc tissue of the backs of the rats. Fifteen male and 15 female rats served as the controls, and their backs were incised but nothing was implanted. Five male and five female rats from each experimental group and three male and three female rats from the control group were killed 3 mo after the treatment and the rest were raised for 2 yr. Sc tumors were produced in 3 male and 5

female rats in group 1, 4 male and 6 female rats in group II, 9 male and 13 female rats in group III, and 1 male and 2 female rats in group IV. Frequency of tumor production differed from group to group; it was greatest in group III, followed by group II and group I, and was lowest in group IV. The period at which the tumor was produced was early in groups III and II and late in group IV. All the tumors were produced where the compounds were implanted. Histologically, most were fibrosarcoma or rhabdomyosarcoma in appearance, and metastasis was observed in some of the cases. Tumors other than sc ones spontaneously occurring in Wistar rats, eg, testicular tumor and leukemia, were observed in the groups, including the control, but there was no difference in their occurrence among the groups. (no Refs)

193 AU - Hasegawa H ; Sato M ; Okonogi K ; Shimaoka A ; Tsuruta H
AD - Natl. Inst. Industrial Health, Kawasaki, Japan
TI - EXAMINATION OF WORKERS IN POLYMERIZATION PROCESS OF VINYL CHLORIDE MONOMER (VCM).
SI - ICDB/80/67206
SO - Ind Health; 17(3):153-185 1979
LA - ENG
AB - Results from several examinations concerning the health of workers involved in VCM polymerization (3 different plants) are presented. Blood of 82 workers and 28 controls was tested biochemically using a battery of 25 screening tests. The amount of VCM in the blood of workers was measured, and the effect of VCM on the activity of a variety of enzymes was statistically analyzed. The metabolic rate of VCM was also determined. (13 Refs)

194 AU - Takahama M ; Nishibe Y ; Shibata T ; Inagaki T
AD - Dept. Pathology, Saitama Medical Sch., Morayama-machi, Saitama Pref 350-04, Japan
TI - MORPHOLOGICAL STUDY OF EARLY LESIONS OF EXPERIMENTAL QUINOLINE-HEPATIC HEMANGIOSARCOMA. COMPARATIVE STUDY WITH VINYL CHLORIDE MONOMER (VCM)-HEPATIC HEMANGIOSARCOMA IN MAN (MEETING ABSTRACT).
SI - ICDB/80/66905
SO - Proceedings of the 38th Annual Meeting of the Japanese Cancer Association held in Tokyo, Japan, September 1979. Japanese Cancer Association, Tokyo, Japan, 321 pp., 1979.
LA - JPN
AB - Three groups of male SD rats that were fed an oriental powder diet containing 0.1% quinoline for 3, 6 and 12 mo, and were killed at the end of administration, and two groups of rats that were fed the same diet for 3 and 6 mo, and killed 12 mo after the start of treatment, were examined by light and electron microscopy. Multiple atypical growth foci of littoral cells were observed only in the group of rats administered quinoline for 12 mo. These atypical cells had carbon inclusive phagocytotic and iron phagocytotic appearance, and many villous cell protrusions were observed in the electron micrographs, which are all characteristic of Kupffer cells. The cases studied in man were liver tissues around the vinyl chloride monomer (VCM)-hepatic

hemangioma and nontumor cases with abnormality in liver tissues and in sinusoid wall cells. There were findings that differed from the victims of VCM poisoning such as the lack of an increase in collagen fibrils around the sinusoidal line. (no Refs)

195 AU - Infante PF
AD - Industry-wide Studies Branch, Natl. Inst. Occupational Safety and Health Center Disease Control, Div. Surveillance, Hazard Evaluation and Field Studies, Cincinnati, OH
TI - EPIDEMIOLOGIC APPROACHES FOR SURVEILLANCE OF GENETIC HAZARDS WITH PARTICULAR REFERENCE TO ANESTHETIC GASES.
SI - ICDB/80/66263
SO - Genetic Damage in Man Caused by Environmental Agents, Proceedings of a Conference held in Oslo, Norway, May 11-13, 1977. Berg K, ed. New York, Academic Press, 551 pp., 1979.
LA - ENG
AB - Genetic hazards due to anesthetic gases are discussed on the basis of epidemiological studies. Studies on spontaneous abortion, birth defects, still births, and birth wt among female anesthetists are reviewed. Studies on spontaneous abortion, birth defects, and decrease in motility of sperm and shape of sperm after male exposure to chloroprene (CP), vinyl chloride (VC), and anesthetic gases are reviewed. Evidence for cytogenetic, mutagenic and reproductive effects of CP and VC is reviewed. (19 Refs)

196 AU - Hansteen IL
AD - Lab. Genetics, Telemark Central Hosp., Porsgrunn, Norway
TI - A FOLLOW-UP STUDY OF PVC WORKERS TWO YEARS AFTER EXPOSURE. PRELIMINARY RESULTS USING SISTER CHROMATIC EXCHANGE FREQUENCY AS AN ASSAY OF GENETIC DAMAGE.
SI - ICDB/80/66262
SO - Genetic Damage in Man Caused by Environmental Agents, Proceedings of a Conference held in Oslo, Norway, May 11-13, 1977. Berg K, ed. New York, Academic Press, 551 pp., 1979.
LA - ENG
AB - Sister-chromatid exchange (SCE) was studied in 16 workers from a polyvinyl chloride (PVC) factory 2 yr after exposure to vinyl chloride monomer (VCM). The study included matched controls from the office employees at the factory. The results showed that the mean number of SCEs per cell was 7.6 for the workers, and 7.5 for the matched controls, indicating that there is probably no difference in the frequency of SCEs between PVC workers and their matched controls. (11 Refs)

197 AU - Doniger DD
AD - Natural Resources Defense Council, Washington, DC
TI - THE LAW AND POLICY OF TOXIC SUBSTANCES CONTROL. A CASE STUDY OF VINYL CHLORIDE.
SI - ICDB/80/62528
SO - The Law and Policy of Toxic Substances Control. A Case Study of Vinyl Chloride. Baltimore, Resources for the Future, 179 pp., 1979.

LA - ENG
AB - The federal regulation of vinyl chloride (VC) is examined to illustrate the complexity of laws and policy relating to toxic substance control in the United States. The still incomplete regulation of VC has involved five major federal agencies operating under 15 separate health and environmental statutes. In 1974, the Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH) learned of the association between VC and angiosarcoma of the liver, and they began preparing a workplace standard for the chemical. The regulation of any toxic substance involves complex decision making under uncertainty, and judgements about the importance of health and environmental values as opposed economic interests. The limits of cancer risk assessment are discussed to explore the nature of scientific uncertainty in the management of hazardous substances. Experimental analysis does not give the regulatory agency a a precise estimate of the risks associated with low doses of substances that are known to cause cancer in humans or in animals at high doses. The limits of economic and technological assessment in determining the costs of controlling exposure to a toxic substance also are reviewed. (85 Refs)

198 AU - Kello D ; Stara JF
AD - Institut za medicinska istrazivanja i medicinu rada, Zagreb, Yugoslavia
TI - HEALTH EFFECT ASSESSMENT OF VINYL CHLORIDE IN THE ENVIRONMENT.
SI - ICDB/80/61795
SO - Arh Hig Rada Toksikol; 30(4):363-397 1979
LA - SCR
AB - Toxicological and hygienic studies of exposure to vinyl chloride (VC) are reviewed. Angiosarcoma of the liver was observed in workers having inhaled VC. Similar and other tumors were found in experimental animals having inhaled or ingested VC. (179 Refs)

199 AU - Ciugudeanu M ; Metes L ; Zugravu E ; Colosi D ; Anca Z ; Gabor S
AU - Preda N ; Suciu L
AD - Institutul de igiena si sanatate publica, Cluj-Napoca, Romania
TI - STUDY OF THE BEHAVIOR OF SOME SERUM ENZYMES IN WORKERS EXPOSED OCCUPATIONALLY TO VINYL CHLORIDE.
SI - ICDB/80/60020
SO - Rev Ig (Ig); 28(8):237-241 1979
LA - RUM
AB - Changes in serum enzyme activities were studied in 84 workers exposed occupationally to vinyl chloride during synthesis. Alkaline phosphatase (AP) was studied in 82 cases, gamma-glutamyl transferase (GGT) in 82, glutamate dehydrogenase (GDH) in 73, SGOT in 84, SGPT in 84, lactate dehydrogenase (LDH) in 76, and cholinesterase (ChE) in 84. Abnormal enzyme activities were found in 6.09% of all patients for AP, in 20.7% for SGGT, in 42.4% for GDH, in 14.2% for SGOT, in 39.2% for GPT, in 5.26% for LDH, and in 3.57% for ChE. In the workers exposed to vinyl chloride less than 10 yr, increased SGPT activity was found, which is indicative of a lesion of the cytoplasm of the hepatocytes. In

workers exposed greater than 10 yr, increased GDH and GGT activities, indicative of more severe lesions of the mitochondrial membranes, were found. The ChE activity was the only parameter to show a slight decrease, whose extent increased with increasing length of exposure. The increase was most pronounced in the SGPT activity for exposures less than 10 yr and in the GDH activity of exposures exceeding 10 yr. (25 Refs)

200 AU - Pialat J ; Pasquier B ; Pahn M ; Kopp N
AD - Laboratoire d'Anatomie Pathologique, CHU de Lyon, Faculte Alexis Carrel, rue Guillaume-Paradin, 69372 Lyon Cedex 2, France
TI - HEPATIC LESIONS CAUSED BY VINYL CHLORIDE MONOMER IN HUMANS. STUDY OF EIGHT CLINICOPATHOLOGICAL CASES.
SI - ICDB/80/59893
SO - Arch Anat Cytol Pathol; 27(6):361-375 1979
LA - FRE
AB - The history of the industrial use of vinyl chloride monomer and the carcinogenic effects in exposed workers is reviewed: eight new cases are reported. The eight patients were all men ranging in age from 38-63 yr. They had been exposed to vinyl chloride fumes in the course of their work for periods of 10-30 yr. Six patients had angiosarcomas of the liver, one had a hepatoma, and one had hepatic fibrosis with portal hypertension. Of the seven patients with neoplasms, five underwent hepatectomy of the involved hepatic lobe; one was alive 18 mo after surgery, but the others died 1 day to 2.5 mo after the surgery. Two patients did not undergo surgery for their liver tumors and lived 2.5 and 8 mo, respectively, after diagnosis. The patient with fibrosis was treated medically and is in good health 2 yr after diagnosis. Histogenic and pathogenic theories of vinyl chloride toxicity are discussed. (111 Refs)

201 AU - Pollice L
AD - Bari, Italy
TI - PRIMARY VASCULAR TUMORS OF THE LIVER (MEETING ABSTRACT).
SI - ICDB/80/59788
SO - Pathology; 165(1/2):145 1979
LA - ENG
AB - The main primary vascular tumors of the liver include cavernous and sclerosing hemangiomas, infantile hemangioendothelioma and angiosarcoma, (so called Kupffer cells sarcoma). On the basis of personal observations and of the data of the literature, n unifying pathogenetic concept of these tumors is proposed. In particular the two different histological patterns of hepatic infantile hemangioendotheliomas are illustrated and their position within an original classification of primary hepatic tumors in infancy and childhood is proposed. Furthermore the oncogenic role played by environmental and occupational agents (namely polyvinyl chloride, thorotrast, arsenical intoxication) on the origin of hepatic angiosarcomas as already reported by several authors, is discussed. Finally, a case of hepatic angiosarcoma, observed in a 26-yr-old man, after a 7 yr period of exposure to acrylonitrile, a vinyl cyanide widely used in the

manufacture of synthetic rubber, is described, and the possible correlations with vinyl chloride induced tumors are proposed. (no Refs)

202 AU - de Laguna JC
AD - No affiliation given
TI - POSSIBLES FACTORES AMBIENTALES EN LA ETIOLOGIA DEL CANCER. [POSSIBLE ENVIRONMENTAL FACTORS IN THE ETIOLOGY OF CANCER].
SI - ICDB/80/56723
SO - Gac Med Max; 115(6):258-263 1979
LA - SPA
AB - The problem of determining causality in the study of cancer was considered. It has been shown that risk of developing lung cancer increases inversely with age at which smoking is begun, directly with the number of cigarettes smoked, and directly with the degree of inhalation. Risk of developing cancer of the mouth increases not only with number of cigarettes smoked per day, but also with quantity of alcohol consumed, and is greatest for those who smoke over 40 cigarettes/day and drink over 1.5 ounces of alcohol/day. Other agents associated with lung cancer include arsenic, asbestos, chrome, carbon, iron oxide, mustard gas, nickel, petroleum, ionizing radiation, and bis-(chloromethyl) ether. Exposure to ionizing radiation and to benzene has been found to increase the incidence of leukemia. Carbon products and aromatic amines have been associated with bladder cancer, arsenic and vinyl chloride with liver cancer, and chrome, isopropyl alcohol, nickel, and the dust of wood and hides with cancer of the buccal cavity and nasal sinuses. Dietary factors including beryllium, lead, arsenic, and iodine are carcinogenic. Deficiencies of iron, molybdenum, magnesium, and zinc are associated with certain cancers. Other carcinogenic substances include fertilizers, pesticides, antibiotics, food additives, aflatoxins, nitrosoamines, and many forms of hormones and pharmaceuticals. Dietary anti-carcinogens include selenium, vitamins C and E, hydroxytoluene, and hydroxyanisole. It was estimated that 99,500/193,600 expected deaths due to cancer could be prevented. (23 Refs)

203 AU - Palmqvist U
AD - Unifos kemi AB, Stenungsund, Sweden
TI - THE LOWEST HARMLESS DOSE IN PRACTICE IS ZERO.
SI - ICDB/80/51804
SO - Kem Tidskr; 91(14):36-40 1979
LA - SWE
AB - Experimental and epidemiological studies on the carcinogenic effects of nitroso compounds and other substances are reviewed. Certain carcinogenic substances, especially nitroso compounds, show a surprising organotropism. Methylalkyl-N-nitrosamine induces tumors of the esophagus, N-methyl-N-nitrosoacetylurea given po causes tumors of the glandular stomach, N-propyl-N-nitrosourea given po induces tumors of the large intestine, N-methyl-N-nitrosourea given iv causes brain tumors, and N-butyl-N-nitrosourea given po causes leukemia. The Ames test

indicates that the active mutagenic substance in a test of vinyl chloride is alpha-chloroacetaldehyde. Tris(2,3-dibromopropyl)phosphate, which contains the carcinogenic impurities 1,2-dibromo-3-chloropropane and 1,2,3-tribromopropane, is also highly mutagenic. (5 Refs)

204 AU - Krahn DF
AD - Haskell Lab. Toxicology and Industrial Medicine, E.I. du Pont de Nemours & Co., Wilmington, DE, 19898
TI - UTILIZATION OF THE CHO/HGPRT SYSTEM: METABOLIC ACTIVATION AND METHOD FOR TESTING GASES.
SI - ICDB/80/51114
SO - Mammalian Cell Mutagenesis: The Maturation of Test Systems. Hsie AW, O'Neill JP, McElheny VR, ed. Cold Spring Harbor, Cold Spring Harbor Laboratory, Banbury Report, No. 2, 504 pp., 1979.
LA - ENG
AB - The use of the CHO/HGPRT (hypoxanthine guanine-phosphoribosyltransferase) assay to study the mutagenic activities of gases, volatile liquids, and chemicals requiring metabolic activation is discussed. The assay yielded reproducible results with structurally diverse chemicals and chemicals requiring activation. The storage of S-9 did not diminish its ability to activate dimethylnitrosamine (DMN), 2-acetylaminofluorene, or 7,12-dimethylbenz(a)anthracene. The mutagenic activity of DMN increased as the concentration of S-9 increased. The proposed procedure for testing gases and volatile liquids proved workable and responded to various compounds as expected on the basis of results from other toxicology tests. However, in contrast to results obtained in microsomal assays with Salmonella typhimurium, vinyl chloride was mutagenic in the CHO/HGPRT system only with a complete activation system. It was concluded that the CHO/HGPRT system in its present form appears to be an appropriate tool for identifying potential mutagens and carcinogens. (8 Refs)

205 AU - Kroes R
AD - No affiliation given
TI - RISKS OF NON-INDUSTRIAL CHEMICAL SUBSTANCES.
SI - ICDB/80/51002
SO - Chemisch Weekblad; 70(51/52):48-50 1979
LA - DUT
AB - The ecological and hygienic problems of toxic and carcinogenic substances in air, water, drinking water, food, and soil are discussed. Acceptable daily intake and relative risk values are given for carcinogenic substances (aflatoxin B1, vinyl chloride, saccharin, cyclamate, and nitrosamines). (12 Refs)

206 AU - Althouse R ; Tomatis L ; Huff J ; Wilbourn J
AD - International Agency for Res. on Cancer., Lyon, France
TI - CHEMICALS AND INDUSTRIAL PROCESSES ASSOCIATED WITH CANCER IN HUMANS. IARC MONOGRAPHS, VOLUMES 1 TO 20.
SI - ICDB/80/49645
SO - IARC Monogr Eval Carcinog Risk Chem (Suppl 1): 71 pp., 1979.
LA - ENG
AB - The program and findings of the International Agency for Research on Cancer (IARC), established in 1917, are summarized. The objective of this program has been to publish monographs on the carcinogenicity of chemicals to which humans are exposed. Data on human and experimental animal carcinogenicity for more than 350 chemicals and industrial processes are evaluated. Human data were available for only 48 chemicals. In 1977, a recommendation was made to regard chemicals known to be carcinogenic in animals as potential human carcinogens, and was adopted beginning with volume 17. Data from the earlier volumes were reevaluated in light of this decision. By the end of 1978, 142 of 442 chemicals and processes evaluated showed carcinogenicity in animals; data on 54 of these chemicals or processes were derived from both human and animal studies. Evidence of carcinogenicity was classified as sufficient, limited, inadequate, negative, or nonexistent. Human data were derived from case reports, epidemiological studies, and case-control and cohort programs. Cause-and-effect was inferred from dose-response relationships. Eighteen chemicals or chemical processes are shown to pose a carcinogenic risk to humans. These include 4-aminobiphenyl, arsenic and certain arsenic compounds, asbestos, manufacture of auramine, benzene, benzidine, N,N-bis(2-chloroethyl)-2-naphthylamine (chlornaphazine), bis(chloromethyl)ether and technical grade chloromethyl methyl ether, chromium and certain of its compounds, diethylstilbestrol, underground hematite mining, manufacture of isopropyl alcohol by the strong acid process, melphalan, mustard gas, 2-naphthylamine, nickel refining, soots, tars, and mineral oils, and vinyl chloride. Eighteen other compounds were judged probably carcinogenic to humans, and eighteen could not be classified. Evidence supporting the evaluations appears in a detailed index. (24 Refs)

207 AU - Resnick MA
AD - Dept. Biochemistry, Coll. Medicine, East Tennessee State Univ., Johnson City, TN
TI - THE INDUCTION OF MOLECULAR AND GENETIC RECOMBINATION IN EUKARYOTIC CELLS.
SI - ICDD/80/49533
SO - Adv Radiat Biol; 8:175-217 1979
LA - ENG
AB - Mechanisms of recombination induction in eukaryotic cells are reviewed. Improved methods for detecting sister chromatid exchanges (SCE) have led to increased interest in the induction of recombination by mutagenic agents. Classically, recombination

has been identified with meiosis, and expression of it manifested in crossing-over during synapsis. Many of the DNA enzymes involved have been found to be common to processes of DNA repair in mitotic cells. Swapping of DNA strand segments leads to formation of hybrid regions. If a mismatched base pair occurs in the hybrid region, it is termed a heteroduplex. Correction leads to gene conversion, or nonreciprocal recombination. Both reciprocal recombination between genes and gene conversion may occur spontaneously in mitotic cells, or may be induced by UV, x-rays, hyperthermia and various mutagens (recombinogens). All chemicals known to be mutagenic in yeast have been found to be recombinogenic as well. Chemicals with both properties include vinyl chloride, mitomycin C, naphthylamines, bleomycin, and formaldehyde. Since most UV-induced recombination can be reversed by photoreactivation, the induced lesions have been presumed to be pyrimidine dimers. Semiconservative replication seems not to be involved in recombination; most evidence indicates a repair function. The spontaneous frequency of recombination is very high in humans with disorders (Blooms syndrome, xeroderma pigmentosum, Fanconi's disease, and ataxia telangiectasia) in which there is also a high incidence of cancer. Studies of recombination may be important for understanding mutagen-induced changes such as tumor induction. (180 Refs)

208 AU - Retv J
AD - Rhone-Poulene Polymeres, 69190 Saint-Fons, France
TI - THE NINTH CASE OF ANGIOSARCOMA OF THE LIVER IN A WORKER IN THE FIELD OF VINYL CHLORIDE POLYMERISATION.
SI - ICDB/80/49516
SO - Arch Mal Prof; 40(6/7):711-743 1979
LA - FRE
AB - A case of liver angiosarcoma in a 63-yr-old man exposed to vinyl chloride for the previous 28 yr is reported. The patient presented with a 18-yr history of intermittent hypochondrium pain, wt loss, and hepatomegaly; 4 yr previously the patient had been treated for jaundice with increased alkaline phosphatase activity. Angiography and aortography showed a well delimited mass in the postero-inferior region of the right lobe of the liver. The patient underwent surgery and three tumoral masses were excised; the left lobe and segment IV were normal. The histological diagnosis of hemangio-endotheliosarcoma was made. The postoperative course was complicated by a biliary fistula and the patient was discharged 4 mo after surgery. Seventeen mo after surgery, the findings of splenic and hepatic scintigraphy were normal. Three mo later, the patient had a recurrence of the fistula, which required surgery, and he died postoperatively. Autopsy showed extensive alterations of liver tissue and the presence of several tumoral nodules (massive angiosarcoma). (no Refs)

209 AU - Popper H ; Thomas LB
AD - Stratton Lab. for Study of Liver Disease, Mount Sinai Sch. Medicine, New York, NY
TI - ENVIRONMENTAL LIVER TUMORS.
SI - ICDB/80/49233
SO - Kurume Med J; 26(3):189-204 1979
LA - ENG
AB - The induction of liver tumors by environmental factors is reviewed, and the significance and incidence of environmental hepatic tumors are presented. Possible factors in the carcinoembryonic chain which determine the development of carcinoma development may be the amount and lifespan of the bioactive agent, the removal or alteration of portions of DNA by endonuclease repair enzymes, and the fixation of DNA alterations. Environmental agents may increase the availability of bioactive metabolites, stimulate hepatocellular proliferation, or serve as the carcinogen. It is noted that there is little evidence of carcinogenicity of polycyclic hydrocarbons and N-nitroso-compounds in humans. The incidence of steroid-induced hepatic tumors that may be due to contraceptive drugs is very low. The characteristic morphologic and clinical sequence associated with vinyl chloride and other agents was presented, and the evolution of human lesions towards angiosarcoma by two different pathways was discussed. Several agents in man elicit sequences of hepatic change which start with mixed nodular hyperplasia and progress to angiosarcoma or hepatocellular carcinoma. (44 Refs)

210 AU - Matos EL
AD - Instituto de Oncologia Angel H. Roffo, Avenida San Martin 5481, 1417 Buenos Aires, Argentina
TI - OCCUPATIONAL CANCER.
SI - ICDB/80/47234
SO - Medicina (B Aires); 39(4):536-539 1979
LA - SPA
AB - Discoveries of carcinogenic substances in occupational environments are reviewed. Since the discovery in 1775 that scrotal cancer occurred with high frequency among chimney sweeps, and the observation in 1895 that workers in the dye industry showed high incidence of bladder cancer, many similar correlations have been made. Recently, the International Agency for the Investigation of Cancer analyzed 380 chemicals or industrial processes and found that 26 were associated with human cancer, 18 of which were involved with occupational hazards. Previous studies have shown that 230 of these chemicals or processes had carcinogenic potential, and 111 were capable of producing malignant tumors in many species and strains. Substances or processes known to cause occupational cancer in man include isopropyl oil and nickel (cancer of the nasal cavity); asbestos, bis-chloromethyl ether, chloromethyl-methyl ether, chromium, mustard gas, hematite, and aromatic polycyclic hydrocarbons in carbon tars (lung cancer); aromatic polycyclic

hydrocarbons in soot and mineral oil, and arsenic (skin cancer); 4-aminobiphenyl, auramine, benzidine, and 2-naphthylamine (bladder cancer); aflatoxin, and vinyl chloride (liver cancer); cadmium (cancer of the prostate); and benzene (cancer of the hematopoietic system). Not all persons exposed to these substances develop cancer. It was suggested that other factors like the inducible hydroxylase of aromatic polycyclic hydrocarbons act upon substances (in this case, particularly benzpyrene) so as to unleash their carcinogenic potential. It is well established that certain diets and smoking can create a microenvironment favorable for tumor development. (19 Refs)

211 AU - Rety J ; Bory RM ; Spay G ; Beurlet J ; Pialat J
AD - Rhone-Poulenc Polymeres, 69190 Saint-Fons, France
TI - THE TENTH FRENCH CASE OF ANGIOSARCOMA OF THE LIVER IN A WORKER EXPOSED TO VINYL CHLORIDE.
SI - ICDB/80/46467
SO - Arch Mal Prof; 40(6/7):743-744 1979
LA - FRE
AB - A 58-yr-old man, who had been exposed to vinyl chloride for the previous 21 yr, was admitted with asthenia, wt loss (3 kg in 3 wk), anorexia, epigastric discomfort, constipation, and increased alkaline phosphatase activity. Laparoscopy showed a hypervascular tumor (8-10 cm) of the right lobe of the liver. The patient underwent right paramedian thoracic laparotomy and hepatectomy. histological diagnosis of angiosarcoma was made, and the patient died of pulmonary embolism 10 days later. (no Refs)

212 AU - Miquet JP ; Allemand H ; Bernard F ; Greff M ; Vuitton D
AU - Gillet M ; Caravon P
AD - Service d'hepato-gastroenterologie, CHU de Besancon, 2, pl. Saint-Jacques, F 25030 Besancon, France
TI - A CASE OF PORTAL HYPERTENSION AND LIVER FIBROSIS FOLLOWING CHRONIC EXPOSURE TO VINYL CHLORIDE.
SI - ICDB/80/46428
SO - Nouv Presse Med; 8(1):3364 1979
LA - FRE
AB - A 46-yr-old man, having 15 yr contact with vinyl chloride, was admitted with ruptured esophageal varicosities, hepatomegaly, splenomegaly, and portal hypertension. The patient underwent surgery and an end-to-end splano-renal anastomosis was performed. Microscopic examination of the liver showed moderate fibrosis. (5 Refs)

213 AU - Du JT ; Sandor JP ; Tseng MT ; Tamburro CH
AD - Div. Digestive Diseases, Nutrition, Univ. Louisville Sch. Medicine, Louisville, KY, 40232
TI - BIOCHEMICAL ALTERATIONS IN LIVERS OF RATS EXPOSED TO VINYL CHLORIDE.
SI - ICDB/80/45375
SO - J Toxicol Environ Health; 5(6):1119-1132 1979
LA - ENG
AB - Male Sprague-Dawley rats were exposed to vinyl chloride (VC) gas

in four experiments (15,000 ppm, 2-8 hr/day, 1-4 wk, total 14-137 hr) to study liver responses in early enzyme changes, the role of the hepatocyte in VC-induced injury and the development of angiosarcoma. Increases in glutathione reductase and glucose-6-phosphate dehydrogenase, and reduction in glucose-6-phosphatase occurred. Light microscopy showed no hepatocellular changes, but electron microscopy revealed dilation of the rough endoplasmic reticulum in some hepatocytes after exposure to VC for 137 hr. There was also an increase in the cytoplasmic density of the affected cells, and other hepatocytes showed small clear patches which tended to aggregate near the cell periphery. The enzymatic changes observed were considered to reflect early hepatocellular adaptations to VC. (41 Refs)

214 AU - de Meester C ; Poncelet F ; Roberfroid M ; Mercier M
AD - Lab. Biotoxicologie, Ecole Pharmacie Univ. Catholique Louvain, 73, Av. E. Mounier, B-1200 Bruxelles, Belgium
TI - VINYL CHLORIDE: DIRECT OR INDIRECT MUTAGEN.
SI - ICDB/80/45284
SO - Arch Int Physiol Biochim; 87(3):620-621 1979
LA - ENG
AB - The substance vinyl chloride (VC) is a reactant in the manufacture of polyvinyl chloride (PVC) used in food packaging. VC increases chromosome aberration rates, and is associated with liver angiosarcoma in those workers exposed to air containing VC. The dependence of VC mutagenicity (M) on metabolic activation was studied using the Ames test, exposing the plates to a 2% VC atmosphere. This mutagenesis appeared to require post-mitochondrial (S9) fractions from mouse liver added to the cultures; these fractions converted VC into an unidentified volatile mutagen. (3 Refs)

215 AU - Asplund I
AD - No affiliation given
TI - LIST OF MAXIMUM ALLOWABLE CONCENTRATIONS FOR AIR POLLUTANTS.
SI - ICDB/80/44290
SO - Kemisk Tidskrift; 91(11):24-27 1979
LA - SWE
AB - The new list of air pollutants which became effective in Sweden on January 1, 1979 is presented. The list includes carcinogenic compounds, such as acrylonitrile, asbestos, benzo(a)pyrene, benzyl chloride, beryllium, dimethylhydrazine, dioxane, hydrazine, chloroform, carbon tetrachloride, 2-nitropropane, polychlorinated biphenyls, trinickel disulfide, and vinyl chloride. Max allowable atmospheric concentrations of these and other compounds are listed. (no Refs)

216 AU - Suskind RR
AD - Inst. Environmental Health Kettering Lab., Coll. Medicine, Univ. Cincinnati, Cincinnati, OH
TI - CUTANEOUS REACTIONS TO COSMETICS.
SI - ICDB/80/43750
SO - J Dermatol (Tokyo); 6(4):203-209 1979
LA - ENG
AB - In general discussion of problems associated with cutaneous reactions to cosmetic preparations and ingredients, it is mentioned that some local skin reactions may be of a photosensitizing nature. Animal and in vitro studies show that certain ingredients of cosmetics may be mutagenic (some permanent hair dyes) or carcinogenic (2,4-toluenediamine and 2,4-diaminoanisole; dioxane and dimethoxane; captan; safrole, isosafrole, and dihydrosafrole; oil of calamus; vinyl chloride; trichloroethylene; and chloroform). (8 Refs)

217 AU - Davis DL ; Magee BH
AD - Toxic Substances Program, Environmental Law Inst., Washington, DC, 20036
TI - CANCER AND INDUSTRIAL CHEMICAL PRODUCTION (LETTER TO EDITOR).
SI - ICDB/80/42914
SO - Science; 206(4425):1356-1357 1979
LA - ENG
AB - Cancer risks associated with industrial chemical production and use were studied to determine regulatory priorities and cancer rates were examined in light of the production histories of industrial carcinogens. It is too soon to reach any conclusions about the magnitude of the cancer risk to the general population posed by industrial chemicals. The annual production of benzene, perchloroethylene, vinyl chloride, acrylonitrile, plastics and resin materials, plasticizers, flavors and perfumes (benzenoid and naphthalenoid), and food, drug, and cosmetic dyes, are shown from 1940 to 1979. Annual and cumulated consumption for chromite and asbestos are shown from 1940 to 1979. (17 Refs)

218 AU - Falk H ; Thomas LB ; Popper H ; Ishak KG
AD - Chronic Diseases Div., Bureau Epidemiology, Center Disease Control, United States Public Health Service, Atlanta, GA, 30333
TI - HEPATIC ANGIOSARCOMA ASSOCIATED WITH ANDROGENIC-ANABOLIC STEROIDS.
SI - ICDB/80/42805
SO - Lancet; 2(8152):1120-1123 1979
LA - ENG
AB - A retrospective epidemiological study of deaths from hepatic angiosarcoma (HAS) in the United States showed that during 1964-74 there were 168 such cases, of which 37 (22%) were associated with previously known causes (vinyl chloride, Thorotrast, and inorganic arsenic) and 4 (3.1%) of the remaining 131 cases with the use of androgenic-anabolic steroids. It is suggested that the long-term use of androgenic-anabolic steroids is the fourth cause of HAS, the majority of cases still being of unknown etiology. Moreover, the presented cases serve as a link

in a spectrum of hepatic disorders recently recognized to be caused by environmental agents such as vinyl chloride, arsenic, and thorotrast, and by contraceptive and anabolic steroids. Similar precursor stages, usually not recognized by clinical laboratory tests and consisting of areas of hyperplasia of hepatocytes and sinusoidal cells and sinusoidal dilatation, lead potentially to hepatic adenoma, carcinoma, peliosis, and angiosarcoma. (Author abstract) (20 Refs)

219 AU - Hinaut G
AD - Service de Pneumologie, CHI de Montfermeil, 10, rue du General Leclerc, F 93370 Montfermeil, France
TI - VINYL CHLORIDE AND POLYVINYL CHLORIDE (LETTER TO EDITOR).
SI - ICDB/80/42509
SO - Nouv Presse Med; 8(40):3271 1979
LA - FRE
AB - Distinction between vinyl chloride and polyvinyl chloride is emphasized in connection with a paper in which the two words were confounded. Polyvinyl chloride contains only infinitesimally small trace amounts of carcinogenic vinyl chloride, if any. (1 Ref)

220 AU - Leoprieno N
AD - Laboratoria di Genetica, Istituto di Antropologia, Univ. Pisa, Pisa, Italy
TI - USE OF YEAST AS AN ASSAY SYSTEM FOR INDUSTRIAL MUTAGENS.
SI - ICDB/80/42328
SO - Chemical Mutagens. Principles and Methods for Their Detection. Hollaender A, de Serres FJ, ed. New York, Plenum Press, Vol. 5, 348 pp., 1979.
LA - ENG
AB - The main features of several genetic systems of yeast that are used to evaluate the mutagenicity of chemical compounds are outlined, and recent findings in different compounds are reviewed. A general diagram of the cell cycle of yeast is presented, and the advantages of using yeast systems are summarized. The types of genetic effects produced by methyl methanesulfonate and the comparative mutagenic effects of chemical and physical agents on Schizosaccharomyces pombe are summarized. The use of yeast to detect mutagenic activity in industrial compounds is discussed with respect to individual compounds. A list of alkylating agents that have been tested for mutagenicity through the reversion of S pombe to arginine independence is presented. Vinyl chloride monomer is discussed in terms of production of point mutations and gene conversions in yeast, in vivo metabolism, and possible active metabolites (2-chloroacetaldehyde, 2-chloroethylene oxide, and 2-chloroethanol). Styrene and styrene oxide are discussed in terms of uses, activation by liver microsomal preparations, and mutagenicity and convertogenicity in yeast. The use of yeast to detect mutagenicity of formaldehyde and trichloroethylene is also described. Pesticides and herbicides are discussed in terms of the mutagenicity of individual compounds, the mutagenicity of

extracts of plants treated with these compounds, and possible genetic risks. Other compounds that have been evaluated in yeast for possible genetic effects are noted and include the chromium salt of potassium, naphthylamines, and hydrogen peroxide. (58 Refs)

221 AU - Bolt HM ; Laib RJ ; Stockle G
AD - Pharmakologisches Institut der Universitat, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany
TI - FORMATION OF PRE-NEOPLASTIC HEPATOCELLULAR FOCI BY VINYL BROMIDE IN NEWBORN RATS (LETTER TO EDITOR).
SI - ICDB/80/41610
SO - Arch Toxicol (Berl); 43:83-84 1979
LA - ENG
AB - In response to an article by Bartsch et al (Arch Toxocol 41, 249-277, 1979) stressing the need for testing the carcinogenic potential of vinyl bromide (VBr), an experiment in which rats were exposed to 2,000 ppm of vinyl chloride (VCl) or VBr (8 hr/day, 5 days/wk) for 4-10 wk or 8-15 wk, respectively, is cited. Histochemical evaluation of ATPase-deficient foci in the livers of the rats 2 wk after cessation of exposure revealed that the oncogenic potential of VBr was approx 1/10 that of VCl. (7 Refs)

222 AU - Thaler H
AD - 4. Medizinische Abteilung, Wilhelminenspital, Montleartstr. 37, A-1171 Wien 16, Austria
TI - HEPATOTOXICITY.
SI - ICDB/80/41575
SO - Dtsch Med Wochenschr; 104(46):1642-1648 1979
LA - GER
AB - Toxic effects manifested in the liver by various drugs and chemicals are reviewed. Hepatotoxicity is discussed in terms of biotransformation, enzyme induction, covalent binding of macromolecules, hepatic kinetics and liver damage, and classification of liver toxins and of liver injuries. A table is presented which summarizes toxic liver damage and typical examples of causes; included are liver cell adenoma caused by ovulation inhibitors, hepatocellular carcinoma caused by aflatoxin B, and angiosarcoma caused by vinyl chloride monomer. Some aspects and causes of hepatotoxicity which are reviewed in detail include the following: cholestasis, peliosis hepatis, focal nodular hyperplasia, changes characteristic of viral hepatitis, allergic hepatitis, and liver necrosis of the type associated with fulminating viral hepatitis. Different types of liver cancer also are considered in detail. The relationship between the use of oral contraceptives or androgens and liver cell adenoma and carcinoma is examined. Adenoma is described with regard to morphology and differentiation from focal nodular hyperplasia. Studies that relate the use of oral contraceptives to the incidence of benign liver tumors, liver cell adenoma, and liver cell carcinoma are summarized. The expected frequencies of occurrence of benign and malignant tumors in women who use oral

contraceptives for greater than 5 yr are noted. Other aspects of liver cancer which are briefly discussed include the mutagenic and carcinogenic effects of active metabolites of aflatoxin B and vinyl chloride monomer. (13 Refs)

223 AU - Czernielewski A ; Kiec-Swierczynska M ; Gluszcz M ; Wozniak L
AD - Dermatological Clinic, Medical Acad., Krzemieniecka 5, Lodz, Poland
TI - DERMATOLOGICAL ASPECTS OF SO CALLED VINYL CHLORIDE MONOMER DISEASE.
SI - CARC/80/07859
SO - Derm Beruf Umwelt; 27(4):108-112 1979
LA - ENG
AB - Dermatological findings in 30 workers (aged 26-54 yr) who had been in close and continuous contact with various phases of the vinyl chloride (VC) polymerization process for 2-11 yr are presented. The most common abnormalities were histopathologic changes (30 workers); history of symptoms of Raynaud's phenomenon (25 workers); positive results in digital plethysmography (24 workers) and in the vibro-tactile threshold sensory test (24 workers); and scleroderma-like skin lesions (23 workers). Acro-osteolysis was found in three patients and thrombocytopenia in one. Most abnormalities disappeared or showed signs of healing within 1-2 yr after exposure was discontinued. These results indicate the importance of dermatological examination in detecting the clinical pattern of VC-induced disease. (32 Refs)

224 AU - Miller RW ; Herrmann J ; Tomatis L ; Infante P
AD - Clinical Epidemiology Branch, Div. Cancer Cause and, Prevention NCI, NIH, Room A-521, Landow Building, Bethesda, MD, 20205
TI - INTRODUCTION: PERINATAL CARCINOGENESIS.
SI - ICDB/80/40450
SO - Natl Cancer Inst Monogr; (51):3-5 1979
LA - ENG
AB - The effects of environmental pollutants (thalidomide, vinyl chloride, dilantin, immunosuppressants, methyl mercury, polychlorinated biphenyls, and polybrominated biphenyls) on human fetuses are discussed. It is suggested that analyses of umbilical cords might lead to greater understanding of the effects of these pollutants on human fetuses. A general discussion is included. (no Refs)

225 AU - Feron VJ ; Spit BJ ; Immel HR ; Kroes R
AD - Dept. Toxicology, Central Inst. Nutrition and Food Res. TNO, P. O. Box 360, 3700 AJ Zeist, Netherlands
TI - ONE-YEAR TIME-SEQUENCE INHALATION TOXICITY STUDY OF VINYL CHLORIDE IN RATS. III. MORPHOLOGICAL CHANGES IN THE LIVER.
SI - ICDB/80/40316
SO - Toxicology; 13(2):143-154 1979
LA - ENG
AB - Morphological changes in the livers of Wistar rats exposed to 0 (control) or 5,000 ppm vinyl chloride monomer (VCM) for 4, 13, 26, and 52 wk were investigated. Livers were examined by light

and electron microscopy, and enzyme histochemical reactions were measured. The major parenchymal changes included swelling and malformation of the mitochondria, an increase in the amount of smooth endoplasmic reticulum, necrosis, nuclear and cellular polymorphism of hepatocytes, foci of cellular alteration, neoplastic nodules, and hepatocellular carcinomas. Glucose-6-phosphatase activity was reduced in the hepatocytes within the foci of cellular alteration, and alkaline phosphatase had a strong sinusoidal activity. In addition to parenchymal alterations, livers of the VCM-exposed animals exhibited focal dilatation of sinusoids, marked alkaline phosphatase activity of sinusoidal cells, focal proliferation of sinusoidal cells with or without atypia, and multicentric angiosarcomas containing widely varying amounts of fibrous tissue. The hepatocytic changes appeared sooner than changes in the sinusoidal lining cells, suggesting that the hepatic parenchyma may have been attacked by VCM before the hepatic stroma was affected. Further clarification of the relationship between hepatocytic and sinusoidal cell alterations is necessary. (33 Refs)

226 AU - Feron VJ ; Kroes R
AD - Dept. Toxicology, Central Inst. Nutrition and Food Res. TNO, P. O. Box 360, 3700 AJ Zeist, Netherlands
TI - ONE-YEAR TIME-SEQUENCE INHALATION TOXICITY STUDY OF VINYL CHLORIDE IN RATS. II. MORPHOLOGICAL CHANGES IN THE RESPIRATORY TRACT, CERUMINOUS GLANDS, BRAIN, KIDNEYS, HEART AND SPLEEN.
SI - ICDB/80/40315
SO - Toxicology; 13(2):131-141 1979
LA - ENG
AB - The morphological changes in the respiratory tract, ceruminous glands, brain, kidneys, heart, and spleen of Wistar rats exposed to atmospheres containing 0 (control) or 5,000 ppm vinyl chloride monomer (VCM) were investigated. Exposure lasted 7 hr/day, 5 days/wk, for 4, 13, 26, and 52 wk. With the exception of one VCM-exposed female rat who had a squamous cell carcinoma arising from the ceruminous gland, treatment-related pathological changes in organs other than the liver were not observed after 4, 13 and 26 wk. A variety of neoplastic and non-neoplastic changes attributed to VCM were observed after 52 wk. In several of the test animals, hyperplastic and neoplastic alterations of the olfactory epithelium in the nasal cavity were observed; the hyperplastic change was proliferation of atypical basal cells and cells of Bowman's glands, and the tumors were highly infiltrative carcinomas. Lesions observed in the ceruminous glands included papillomas, squamous cell carcinomas, and adeno-squamous carcinomas. Primary tumors were found in the lungs of two rats and were identified as a papillary adenoma and a mesenchymal type tumor. Some test animals had deformed noses due to small focal swellings suggestive of nasal tumors, while at least 20 test animals had malignant nasal tumors. One primary brain tumor was found in the anterior part of the cerebrum. Other brain tumors were observed but were determined to be metastases from other primary locations. Hemorrhage and inflammatory changes were

observed in the lungs of several rats with brain tumors or with pulmonary metastases from liver tumors. (25 Refs)

227 AU - Mangler LW ; Rogozen MB ; Ziskind RA ; Reynolds R
AD - Science Applications, Inc., Los Angeles, CA
TI - RAPID SCREENING AND IDENTIFICATION OF AIRBORNE CARCINOGENS OF GREATEST CONCERN IN CALIFORNIA.
SI - ICDB/80/37221
SO - J Air Pollut Control Assoc; 29(11):1153-1157 1979
LA - ENG
AB - A method for establishing a priority list of airborne carcinogens within a state jurisdiction is described. The California Air Resources Board (CARB) is sponsoring a three-stage study of airborne emissions of carcinogens. The initial screening procedure identified known or suspected carcinogens most likely to be hazardous to the general population of California. The 22 materials identified were ranked by additive and multiplicative algorithms. Criteria used in the ranking procedure included present use and growth in use in California, emission potential, stability in ambient air, dispersion potential, and evidence of carcinogenicity. A nine-member panel of governmental, industrial, and academic scientists also evaluated and ranked the materials. The final selection consisted of 11 substances appearing on at least 2/3 lists and included, in alphabetical order, arsenic, asbestos, benzene, cadmium, carbon tetrachloride, chloroform, ethylene dibromide, ethylene dichloride, nitrosamines, perchloroethylene, and polycyclic aromatic hydrocarbons. Other highly ranked carcinogenic substances not included on the list were those already subject to established standards (vinyl chloride) or containing substances included on the final list (gasoline, tobacco smoke). In continuing studies, a baseline emissions inventory is being prepared, and a source testing program is being designed. (16 Refs)

228 AU - Kucerova M ; Polivkova Z ; Batora J
AD - Katedra pediatrie, Institut pro dalsi vzdelavani lekaru a farmaceutu, Budejovicka 800, Prague 4, Czechoslovakia
TI - MUTAGENIC AND CARCINOGENIC EFFECTS OF VINYL CHLORIDE.
SI - CARC/80/07526
SO - Prac Lek; 31(6/7):249-252 1979
LA - CZE
AB - The mutagenicity of vinyl chloride (VC) was studied in peripheral blood lymphocytes of nine workers at a polyvinyl chloride manufacturing plant. The workers have been exposed to VC at concentrations of 15-150 ppm for 10-25 yr. Two of three cytogenetic examinations performed over a 2-yr period did not reveal any significant increase in the percentage of cells with chromosome aberrations compared with that in eight nonexposed controls; the final test, however, showed a significant increase in the percentage of cells with chromosome aberrations in three workers (5.2% vs 1.8% in the controls). The sister chromatid exchange (SCE) test was also performed at the time of the third test: it demonstrated significant increases in SCE frequency in

5/7 tested workers (13.8% vs 9.41% in the controls). (23 Refs)

229 AU - Milby TH
AD - Div. Scientific and Educational Activities, California Medical Assoc., 731 Market St., San Francisco, CA, 94103
TI - VINYL CHLORIDE-RELATED CANCER.
SI - CARC/80/07502
SO - West J Med; 130(3):247-248 1979
LA - ENG
AB - Vinyl chloride (VC) has been shown to cause cancer as well as a number of toxic, nonmalignant diseases in man. There is also some evidence that workers exposed to VC may have an increased frequency of chromosomal aberrations. Angiosarcoma of the liver has been diagnosed in numerous workers exposed to VC, as have CNS tumors (particularly glioblastoma multiforme), lung cancer, and cancers of the lymphatic and hematopoietic systems; liver and biliary cancers show a possible association with VC exposure. (1 Ref)

230 AU - Barndt H
AD - Dept. Internal Medicine, County Hosp. with Polyclinic, Neubrandenburg, E. Germany
TI - CURRENT PROBLEMS OF SOLID HEPATIC TUMORS.
SI - ICOB/80/36209
SO - Cesk Gastroenterol Vyz; 33(4):220-229 1979
LA - CZE
AB - The etiological, epidemiological, and clinical aspects of solid hepatic tumors are reviewed. Correlation between oral contraception and benign hepatocellular tumors was demonstrated in numerous studies. Significant correlation was found between hepatic cancer and hepatitis B infection in Senegal. Vinyl chloride has been demonstrated as an occupational etiological factor in angiosarcoma of the liver. The incidence of primary malignant hepatic carcinoma is highest in Africa and the Far East, in which aflatoxins are a major factor. The incidence among Afroamericans is about the same as in American whites, which indicates the etiological role of environmental factors. Wt loss, weakness, loss of appetite, hepatomegaly, and tenderness of the liver are the major clinical symptoms of liver cancer. Pathologically increased alpha-fetoprotein levels were found in 38-87% of the hepatoma patients and in 0-10% of healthy controls in various studies. Radical surgery is the treatment of choice in hepatoma. (64 Refs)

231 AU - Karlowski K ; Mazur H ; Jedrych Z
AD - Zaklad Badania Zywnosci i Przedmiotow Uzytku, Panstwowy Zaklad Higieny, ul. Chocimska 24, 00-791 Warsaw, Poland
TI - A METHOD FOR THE DETERMINATION OF VINYL CHLORIDE IN PLASTIC MATERIAL USED IN FOOD PACKAGING.
SI - CARC/80/07429
SO - Rocz Panstw Zakl Hig; 30(4):371-376 1979
LA - POL
AB - A method for the determination of vinyl chloride (VC) and

polyvinyl chloride (PVC) is reported. PVC is dissolved in tetrahydrofuran, and the monomer content in the distilled solvent is determined by gas chromatography with flame-ionization detection. The recovery rate ranged from 0.05 to 100 mg/kg for VC and from 61% to 80% for PVC. The detectability index for VC was 0.01 mg/kg of plastic material. (14 Refs)

232 AU - Sadowski S
AD - Zaklad Higieny Komunalnej, Panstwowy Zaklad Higieny, ul. Chocimska 24, 00-791 Warsaw, Poland
TI - DETERMINATION OF LOW CONCENTRATIONS OF VINYL CHLORIDE IN THE AIR.
SI - CARC/80/07424
SO - Roczn Panstw Zakl Hig; 30(4):413-419 1979
LA - POL
AB - A method for the determination of low concentrations of vinyl chloride in the air is reported. The method is based on the adsorption of vinyl chloride on activated charcoal followed by de-absorption of the carbon with carbon disulfide. Vinyl chloride is then determined by gas chromatography and a flame-ionization detector. The limit of detection of the method is 0.1 ng vinyl chloride. (14 Refs)

233 AU - Hopkins J
AD - No affiliation given
TI - VINYL CHLORIDE--PART 1: METABOLISM.
SI - CARC/80/07396
SO - Food Cosmet Toxicol; 17(4):403-405 1979
LA - ENG
AB - The metabolism of vinyl chloride (VC) is reviewed. The metabolism of VC administered to rats by various routes appears to be dose-related, the major urinary metabolites being N-acetyl-S-(2-hydroxyethyl)cysteine, N-acetyl-S-vinylcysteine, and thiodiglycollic acid. Chloroacetic acid does not appear to be a major VC metabolite. A cytochrome enzyme is involved in the formation of the active metabolites, and there appears to be only a single saturable metabolic pathway for VC in the rat. (12 Refs)

234 AU - van Lierop JB
AD - Keuringsdienst van Waren, Utrecht, Netherlands
TI - SUBSTANTIAL REDUCTION IN THE LEVELS OF CARCINOGENIC SUBSTANCES IN FOOD PACKAGING MATERIALS.
SI - CARC/80/07379
SO - Voedings Middelen Technol; 12(11):29 1979
LA - DUT
AB - The vinyl chloride residue level in food packaging materials has decreased substantially from 127 ppm in 1974 to 77 ppb in 1978 in the Netherlands. The max allowable vinyl chloride concentration in food is 10 ppb. (no Refs)

235 AU - Binns CH
AD - Medical Centre, BP Oil Ltd., BP House, Victoria St., London, SW1E 5NJ, England
TI - VINYL CHLORIDE: A REVIEW.
SI - ICDB/80/36154
SO - J Soc Occup Med; 29(4):134-141 1979
LA - ENG
AB - The chronology of events leading to the association of vinyl chloride with acro-osteolysis and with angiosarcoma of the liver is outlined, and the epidemiological, chemical, histopathological, and biochemical investigations that resulted are reviewed. Clinical manifestations of vinyl chloride exposure are acro-osteolysis, angiosarcoma of the liver, hepatic fibrosis, pulmonary adenomas, cerebral neuroblastomas, mutagenicity, chromosomal aberrations, embryotoxicity, and teratogenicity. The metabolism of vinyl chloride and possible mechanisms of action which would account for the clinical effects are discussed. (50 Refs)

236 AU - Falk H ; Thomas LB ; Popper H ; Ishak K
AD - Center for Disease Control, Atlanta, GA
TI - HEPATIC ANGIOSARCOMA ASSOCIATED WITH USE OF ANDROGENIC-ANABOLIC STEROIDS (MEETING ABSTRACT).
SI - ICDB/79/35758
SO - Gastroenterology; 77(5):A11 1979
LA - ENG
AB - A retrospective epidemiologic study of deaths from hepatic angiosarcoma in the United States in the period 1964 through 1974 identified 168 cases; of these, 37 (22%) were associated with previously known causes (vinyl chloride, Thorotrast, and inorganic arsenic). Of the remaining 131 cases, 4 (3.1%) were associated with the use of androgenic-anabolic steroids; available drug use data suggest that this proportion is higher than expected. It is postulated that the long-term use of androgenic-anabolic steroids is a fourth cause of hepatic angiosarcoma, with the majority of cases still of unknown etiology. Moreover, the presented cases serve as a link in a spectrum of hepatic disorders recently recognized to be caused by environmental agents such as vinyl chloride, arsenic, and Thorotrast, and by contraceptive and anabolic steroids. Similar precursor stages, usually not recognized by clinical laboratory tests, consisting of areas of hyperplasia of hepatocytes and sinusoidal cells and sinusoidal dilatation lead potentially to hepatic adenoma, carcinoma, peliosis, and angiosarcoma. (no Refs)

237 AU - Bognar Z ; Czeizel E ; Szentesi I
AD - Schopf-Merei Korhaz es Anyavedelmi Kozpont, Orszagos Kozegeszegugyi Intezet, Hungary
TI - EPIDEMIOLOGICAL STUDY OF THE REPRODUCTIVE FUNCTION IN PVC WORKERS.
SI - CARC/79/07174
SO - Orv Hetil; 120(30):1819-1821 1979
LA - HUN
AB - An epidemiological study of the families of 231 workers exposed to polyvinylchloride (PVC) or vinyl chloride showed an increase in the frequency of miscarriage, intrauterine death, and congenital anomalies (eg, spina bifida) in the families of workers exposed to vinyl chloride compared with families of nonexposed controls and families of workers exposed to PVC. (20 Refs)

238 AU - De Meester C ; Duverger-Van Bogaert M ; Lambotte-Vandepaer M
AU - Roberfroid M ; Poncelet F ; Mercier M
AD - Lab. Biotoxicology, Sch. Pharmacy, Univ. Louvain, U.C.L.-73.69, B.1200 Brussels, Belgium
TI - LIVER EXTRACT MEDIATED MUTAGENICITY OF ACRYLONITRILE.
SI - ICDB/79/34490
SO - Toxicology; 13(1):7-15 1979
LA - ENG
AB - The mutagenic effect of acrylonitrile (ACN) vapors on Salmonella typhimurium and the enhancement of mutagenicity by liver postmitochondrial fractions were studied. Adult rats and mice were pretreated as follows: daily ip injection of diethylmaleate (DEM), arochlor (ARO), phenobarbital (PB), 3-methylcholanthrene (3-MC), acrylonitrile (ACN), or styrene (STY); inhalation of vapors of butadiene (BUT), vinyl chloride (VCM), or vinylidine chloride (VDC); and consumption of drinking water containing PB. The livers were removed, homogenized, and centrifuged to obtain the postmitochondrial fraction S9. Microsomes P/4 and cytosols S/10 were added to the mix at the same concentration as S9; the P/4 mix was further supplemented with glucose-6-phosphate dehydrogenase. S typhimurium strains TA 1530 and TA 1538 were incubated for 1 hr in the presence of ACN after the addition of S9, P/4, or S/10. The numbers of his+ revertant colonies were calculated. The liver postmitochondrial fractions from mice had a more pronounced effect on the mutagenicity of ACN than did those from rats. Pretreatment with DEM, PB, or ACN decreased the mutagenicity of ACN when the S9 fraction was obtained from rats and increased the mutagenicity of ACN when the S9 fraction was obtained from mice. Pretreatment with STY, VCM, VDC, BUT, and 3-MC increased the mutagenicity of ACN when S9 was obtained from both rats and mice. Pretreatment did not affect the protein concentrations of the various S9 fractions; within the range of S9 concentrations used (30-240 ul S9/plate), the number of his+ revertants/plate increased with the protein concentration. The reversion rate was unaffected by the addition of valeric acid (SKF 525A) or by inactivation of cytochrome P450 by previous incubation of the S9 mix with carbon monoxide. In contrast, the

mutagenic effect of ACN was completely inhibited by the addition of metyrapone or by boiling the S9 mix. The results suggest that the cytochrome P450-dependent monooxygenases do not play a major role in the metabolic activation of ACN into a mutagenic intermediate. (19 Refs)

239 AU - Poncelet F ; De Meester C ; Roberfroid M ; Mercier M
AD - Lab. Biotoxicology, Sch. Pharmacy, Brussels, Belgium
TI - INFLUENCE OF EXPERIMENTAL FACTORS ON THE MUTAGENICITY OF VINYLIC MONOMERS (MEETING ABSTRACT).
SI - ICDB/79/33771
SO - 21st Congress of the European Society of Toxicology held in Dresden, E. Germany, 11-13 June 1979. European Society of Toxicology:, 194 pp., 1979.
LA - ENG
AB - The mutagenicity of several vinylic monomers such as styrene, butadiene, acrylonitrile, and vinyl chloride was evaluated with the Salmonella typhimurium test system in various experimental conditions: the classical plate incorporation method, incubation in liquid medium, exposure in gaseous atmospheres or a bacterial fluctuation test. Morever, assays were performed in the presence of different metabolic activating systems: liver post-mitochondrial fractions, liver purified microsomal fractions obtained from variously pretreated animals of different species (rats, mice, etc); morever, the protein content of the suspensions utilized as enzyme sources was varied. The results obtained clearly demonstrate that all these experimental parameters have a very profound and variable effect on the mutagenic potency of these monomers. The magnitude of the modification seems to be frequently correlated with the physico-chemical properties of the monomer assayed. (1 Ref)

240 AU - Laipold-Angermuller S ; Wagener K
AD - No affiliation given
TI - DOUBLE TUMORS OF THE LIVER FOLLOWING INTRAVENOUS INJECTION OF THOROTRAST (MEETING ABSTRACT).
SI - ICDB/79/33572
SO - Zentralbl Allg Pathol; 123(3):278 1979
LA - ENG
AB - The rare simultaneous existence of a cholangio-cellular carcinoma (CCC) and a hemangioendotheliosarcoma (HeSA) in each of two patients who had previously received iv injections of Thorotrast is reported. Thirty-five yr after injection of Thorotrast, a man developed infiltrating CCC with metastases to the lung and adrenal gland. Single polymorphic and hypochromatic cells were distributed in the wall of a hyperemic and dilated sinus. Similar proliferations of polymorphic and hypochromatic cells have been seen in the early stages of development of HeSA in workers who have been exposed to vinyl chloride. The patient died of tumor-induced shock at the age of 63 yr. A woman developed a nonmetastasizing CCC and an infiltrating, destructive HeSA showing similarities to the areas containing the aberrant sinus-wall cells in the first patient. Other areas resembled

small pools of blood, but most contained a network of tumor cells with various types of atypical cells. The woman died at the age of 47 yr in hypovolemic shock. Thorotrast was not found in either the proliferating sinus-wall cells or in the HeSA tumor cells. (no Refs)

241 AU - Roosken AA
AD - Dienst Centraal Milieubeheer Rijnmond, Schiedam, Netherlands
TI - MEASURING ORGANIC GASES AND VAPORS IN THE AIR.
SI - ICDB/79/32904
SO - Polytech Tidschr Procestechniek; 34(7):409-415 1979
LA - DUT
AB - The measurement of organic gases and vapors in the atmosphere is described, and the problems of air pollution caused by organic emissions in South Holland are outlined. Considerable amounts of vinyl chloride, benzene, and acrylonitrile are emitted from in an industrial area in South Holland. Measuring the total amount of hydrocarbons is the simplest method to determine organic gases and vapors in the air. The individual components can be identified by the combination of mass spectrometry with capillary gas chromatography, or by determining the retention time. Vinyl chloride can be determined by gas chromatography. (15 Refs)

242 AU - Aune T
AD - Miljotoksikologisk avdeling, Statens Institutt for Folkehelse, Oslo, Norway
TI - CARCINOGENIC CHEMICALS IN THE ENVIRONMENT.
SI - CARC/79/06914
SO - Kjemi; 39(5):25-29 1979
LA - NOR
AB - Recent studies on environmental carcinogens are reviewed. The chemical substances known to be carcinogenic in humans include aflatoxins, 4-aminobiphenyl, arsenic compounds, substances occurring in the synthesis of auramine, benzene, benzidine, bis(chloromethyl) ether, cadmium, chloramphenicol, chloromethyl methyl ether, chromium, cyclophosphamide, diethylstilbestrol, isopropyl oils, Melphalan, mustard gas, 2-naphthylamine, nickel, N,N-bis(2-chloroethyl)-2-naphthylamine, oxymetholone, phenacetin, soot, tar, and vinyl chloride. The mutagenicity of cigarette smoke condensate cannot be explained with the presence of benzopyrene and nitrosamines alone. There are strong indications that the pyrolysis products of proteins and amino acids contribute substantially to the mutagenic effect. It cannot be ruled out that such cocarcinogens as harman and norharman also play an important role. Chemically induced cancer is dose-dependent, even though the dose-response relationship for humans is not yet known for the concentrations that are relevant for human exposure. The fact that a chemical induces cancer in animals or mutations in other test systems is not always sufficient substantiation for the ban of that substance. (6 Refs)

243 AU - Jukes TH
AD - Univ. California, Berkeley, CA, 94704
TI - DDT AND CANCER.
SI - CARC/79/06899
SO - Clin Toxicol; 14(4):461-463 1979
LA - ENG
AB - The claim that DDT exposure causes cancer is disputed. DDT feeding in rats for 2 yr (most of the rat lifespan) results in a minimal hepatocarcinogenic tendency. Liver changes identical to those produced by phenobarbital, pyrethrum, and other chemicals were seen 14 wk after DDT feeding in rats and could be produced in rabbits, mice and guinea pigs, but not in chickens, dogs, cats, and monkeys or large domestic animals. In another study, no tumors were found in three generations of dogs (greater than 500 animals) raised on diets containing high DDT doses. Factory workers in DDT production and men who have been involved in spraying DDT for many years have shown no indication of DDT causing cancer. This is in marked contrast to other industrial carcinogens, including asbestos, arsenic, vinyl chloride, and dimethylchlorether. According to the World Health Organization, extensive medical tests of 150 persons with prolonged occupational exposure to large doses of DDT have not revealed any related findings except increased storage and excretion of DDT and its metabolites and mild stimulation of hepatic microsomal enzymes. (no Refs)

244 AU - Reitz RH ; Quast JF ; Watanabe PG ; Gehring PJ
AD - Toxicology Res. Lab., Health and Environmental Sciences, U.S.A., Dow Chemical U.S.A., 1803 Building, Midland, MI, 48640
TI - CHEMICAL CARCINOGENS: ESTIMATING THE RISK (LETTER TO EDITOR).
SI - ICDB/79/31810
SO - Science; 205(4412):1206-1208 1979
LA - ENG
AB - Although it is believed to be possible that thresholds for chemical carcinogens exist, research on vinyl chloride has not provided evidence showing such thresholds. Attempts to provide irrefutable evidence of absolute thresholds for chemical carcinogens are viewed as futile. Moreover, it is emphasized that risk assessment should be tested against real work related data when ever possible. (11 Refs)

245 AU - Hesbert A ; Cavelier C ; Bottin MC ; Lemonnier M
AD - Institut National de Recherche et de Securite, avenue de Bourgogne, B.P. no. 27, 54500 Vandoeuvre-les-Nancy, France
TI - MUTAGENIC EFFECT OF A CHEMICAL ON BACTERIAL STRAIN OF SALMONELLA TYPHIMURIUM (AMES TEST): METHOD AND RESULTS FOR SEVERAL KNOWN CARCINOGENS.
SI - CARC/79/06758
SO - Arch Mal Prof; 40(3/4):437-457 1979
LA - FRE
AB - The mutagenicity of known chemical carcinogens was tested using the Salmonella typhimurium strains TA 98, TA 100, TA 1538, TA

1535, TA 1537, and TA 1530, with and without metabolic activation by rat hepatic microsomal fraction. Ames test results were considered positive if the number of revertants per dish exceeded double the number of spontaneous revertants. All substances tested (2-aminofluorene, 2-acetylaminofluorene, 9-aminoacridine, 1-aminoanthracene, 2-aminoanthracene, dibenzo(a,i)pyrene, benzo(a)pyrene, 3-methylcholanthrene, chrysene, 7,12-dimethylbenz(a)anthracene, 4-nitroquinoline-1-oxide, N-methyl-N'-nitro-N-nitrosoguanidine, methylmethane sulfonate, sodium azide, aflatoxin B1, and vinyl chloride were found to be mutagenic, both with and without metabolic activation. (14 Refs)

246 AU - Pilichowski P ; Faure C ; Aubert M ; Pahn M ; Latreille R
AU - Barrie J
AD - Service de Chirurgie Thoracique, Hopital des Sablons, F 38700 La Tronche, France
TI - ANGIOSARCOMA OF THE RIBS ASSOCIATED WITH POLYVINYL CHLORIDE INTOXICATION.
SI - ICDB/79/30442
SO - Nouv Presse Med; 8(30):2485 1979
LA - FRE
AB - A 38-yr-old man, who had worked many years in a vinyl chloride factory, presented with a 4-mo history of left thoracic pain. Radiography showed an area of lysis on the posterior arch of the fifth rib and on the seventh dorsal vertebra (without associated spondylodiscitis). The patient underwent surgery (excision of the posterior arches of the 4th, 5th, and 6th ribs). A diagnosis of angiosarcoma, beginning to invade the soft tissues, was made. Scintigraphy and angiography revealed a malignant tumor in the right lobe of the liver. Two mo after surgery, lysis of third left rib was observed. The patient died 2 mo later, after suffering hemorrhagic collapse (rupture of the hepatic tumor) and right hepatectomy. (4 Refs)

247 AU - Powell-Jackson P ; Davis M
AD - Liver Unit, King's Coll. Hosp., Denmark Hill, London, England
TI - OCCUPATIONAL LIVER DISEASE.
SI - ICDB/79/29907
SO - Practitioner; 223(1333):67-70 1979
LA - ENG
AB - Occupational hepatotoxins are classified according to the nature of the liver injury that each causes. Acute hepatocellular injury is caused by carbon tetrachloride, tetrachloroethane, toluene, trichloroethylene, 2,2bis(p-chlorophenyl)-1,1,1-trichlorethane, trinitrotoluene, ionizing radiation, hepatitis B virus, and halothane. Granulomatous hepatitis is caused by beryllium, and hepatic fibrosis and malignancy are caused by vinyl chloride monomer. (39 Refs)

248 AU - Pessayre D ; Wandscheer JC ; Descatoire V ; Artigou JY
AU - Benhamou JP
AD - Unite de Recherches de Physiopathologie Hepatique, Hospital Beaujon, 92118 Clichy, France
TI - FORMATION AND INACTIVATION OF A CHEMICALLY REACTIVE METABOLITE OF VINYL CHLORIDE.
SI - ICDB/79/29519
SO - Toxicol Appl Pharmacol; 49(3):505-515 1979
LA - ENG
AB - The metabolic activation of vinyl chloride by hepatic microsomal mixed-function oxidase system into chemically reactive metabolites that 1) covalently bind in vitro to microsomal proteins, 2) covalently bind in vivo to tissue proteins, and 3) may destroy hepatic cytochrome P-450 and deplete hepatic glutathione was studied in both non-treated and in variously treated male Sprague-Dawley rats. When the rats were exposed to a 5% vinyl chloride atmosphere for 18 hr, the hepatic microsomal cytochrome P-450 decreased linearly with time; the decrease was negligible in rats treated with cobalt chloride (CoCl2), but higher in phenobarbital-treated rats. 14C-vinyl chloride administration resulted in irreversible radioactive binding to whole tissue proteins: binding to blood, kidney, and spleen proteins was about 33% of that to liver proteins; CoCl2 reduced binding in all organs tested. When 14C-vinyl chloride was incubated with hepatic microsomes and the NADPH-regenerating system, radioactive binding to microsomal proteins was detected, whereas no binding occurred with microsomes from blood, kidney, spleen, or muscle. No binding to hepatic microsomal proteins was detected in the absence of the NADPH-regenerating system or in the presence of 90% carbon monoxide-10% oxygen atmosphere or SKF 525-A. In vitro binding to hepatic microsomes was decreased by glutathione or cysteine, but not S-methyl glutathione or glycine. Addition of the compound 1,1,1-trichloropropene 2,3-oxide (TCPO) to the incubation mixture increased in vitro binding to microsomes; and whereas binding was increased by only 37% in control rats, it was increased by 134 and 200% in phenobarbital treated rats, respectively. (28 Refs)

249 AU - Maltoni C
AD - Inst. Oncology, Tumor Center, Bologna, Italy
TI - PERSPECTIVES ON ENVIRONMENTAL AND OCCUPATIONAL ONCOGENESIS OF CNS (MEETING ABSTRACT).
SI - ICDB/79/29293
SO - International Symposium on Multidisciplinary Aspects of Brain Tumor Therapy. Abstracts of a Symposium held in Brescia, Italy, 8-10 June 1979. To be published by Elsevier/North-Holland Biomedical Press, Amsterdam, 156 pp., 1979.
LA - ENG
AB - Tumours of CNS in humans have not been correlated in the past with environmental oncogenic factors. The only available data, before 1970, were the results of an epidemiological investigation indicating an excess of CNS tumors among workers in the rubber

and plastic industries, in Ohio, the center of the United States rubber industry. In recent yr, the hypothesis of possible environmental origin of CNS as well as of other neurogeneous tumors has been growing on the basis of three sets of results. 1) Vinyl chloride, one of the most important compounds in the plastic industry, given by inhalation, produces encephalic neuroblastomas in rats. Parallely, a fivefold incidence of brain neoplasias has been reported among workers heavily exposed to this monomer. 2) Acrylonitrile, another very important compound in plastic industry, administered by ingestion and by inhalation, causes CNS gliomas in rats. 3) Bis(chloromethyl)ether, administered by inhalation, produces in rats esthesioneuroepitheliomas. On the basis of these recent findings, the following conclusions can be reached: 1) CNS tumors may be environmental in origin; 2) the possible carcinogenic effects on the CNS of known and suspected carcinogens must be better explored, both experimentally and epidemiologically; 3) more basic research in experimental animals should be performed, with particular regard to natural incidence of CNS tumors. (no Refs)

250 AU - Bartsch H ; Sabadie N ; Malaveille C ; Camus AM ; Brun G
AD - Unit Chemical Carcinogenesis, International Agency Res. Cancer, 69008 Lyon, France
TI - TISSUE SPECIFICITY IN METABOLIC ACTIVATION.
SI - CARC/79/06078
SO - Adv Pharmacol Chemother; 9:93-102 1979
LA - ENG
AB - A model for the organospecificity of chemicals is proposed based on data from several systemically acting carcinogens: N-nitrosamines, N-(alpha-acyloxy)alkyl-N-alkylnitrosamines, and 3,3-dimethyl-1-phenyltriazene. The organ specificity of certain carcinogenic chemicals can be determined by the half-lives of their ultimate carcinogens, which may act to prevent their distribution in the body by covalent reactions in the organs (cells) in which they are generated. In human liver, large interindividual differences in the activity of carcinogen-activating enzymes were noted. Aryl hydrocarbon-hydroxylase (AHH) activity and microsome-mediated mutagenicity were measured using the hepatocarcinogens N-nitrosomorpholine, N-nitroso-N'-methylpiperazine, and vinyl chloride as substrates. When AHH activity in liver specimens from human subjects was plotted against the respective microsome-mediated mutagenicity for Salmonella typhimurium, a positive correlation was obtained for the rate of oxidative benzo(a)pyrene metabolism and mutagenicity in the presence of all three substrates. Thus, differences in tissue-specific activation processes of chemical carcinogens appear to be contributing factors in the production of tumors on in certain organs and may also condition the carcinogenic response in different individuals when they are exposed to the same level of environmental carcinogens. (34 Refs)

251 AU - Henschler D ; Bonse G
AD - Inst. Toxicology, Univ. Wurzburg, D-8700 Wurzburg, W. Germany
TI - METABOLIC ACTIVATION OF CHLORINATED ETHYLENE DERIVATIVES.
SI - CARC/79/06075
SO - Adv Pharmacol Chemother; 9:123-130 1979
LA - ENG
AB - The chlorinated ethylenes (CE) were studied to determine the structural requirements for their oncogenic effects. The epoxides of all CEs except 1,1-dichloroethylene oxide were prepared, and the in vitro rearrangement mechanisms were studied. The epoxide rearrangement products were either chlorinated aldehydes or acyl chlorides. The metabolites excreted in vivo, chlorinated ethanols and acetic acids, can be derived from the epoxide rearrangement products. Trichloroethylene was an exception; its epoxide rearranged in vitro to dichloroacetyl chloride, whereas the metabolites are oxidation or reduction products, respectively of trichloroacetaldehyde. In vivo, trichloroethylene epoxide is converted, via the trivalent iron of cytochrome P450, at the site of formation in the hydrophobic phase to chloral. In a modified Ames test system using Escherichia coli K 12, vinyl chloride, vinylidine chloride, and trichloroethylene exerted mutagenic activity after activation by induced liver microsomes. The tetra- and 1.2-dichloroethylenes (cis and trans) were inactive in this system. A molecular rule derived from these findings states that unsymmetric chlorine substitution induces, by an imbalanced electron withdrawing effect, the epoxides to become highly electrophilic, this being a prerequisite for mutagenicity and carcinogenicity. (18 Refs)

252 AU - Sullivan FM ; Barlow SM
AD - Dept. Pharmacology, Guy's Hosp. Medical Sch., St. Thomas St., London SE1 9RT, England
TI - CONGENITAL MALFORMATIONS AND OTHER REPRODUCTIVE HAZARDS FROM ENVIRONMENTAL CHEMICALS.
SI - CARC/79/06037
SO - Proc R Soc Lond [Biol]; 205(1158):91-110 1979
LA - ENG
AB - Possible adverse effects of chemical exposure on reproduction are discussed, and data concerning the reproductive outcome after exposure to chemicals in the workplace or environment are reviewed. Exposure of men to environmental chemicals may lead to cancer in their offspring; a study of 386 children dying from malignant disease before less than 5 yr of age showed a significant excess of fathers in hydrocarbon-related occupations. The association between vaginal cancer and prenatal diethylstilbestrol exposure has been established. Angiosarcomas have been reported in offspring of pregnant rats exposed to vinyl chloride monomer. Other possible transplacental carcinogens include anesthetics and irradiation. (103 Refs)

253 AU - Frejaville JP ; Beaune P ; Cresteil T
AD - Departement d'Anesthesiologie, Hopital Necker, 49, rue de Sevres, 75015 Paris, France
TI - METABOLISM OF CHLOROETHYLENES.
SI - ICDB/79/26806
SO - Arch Mal Prof; 40(1/2):359-364 1979
LA - FRE
AB - Current data on the human metabolism of trichloroethylene and vinyl chloride are reviewed. The metabolic pathways and potential carcinogenicity of their degradation products are discussed, and their replacement by tetrachloroethylene or 1,2-dichloroethylene is advised. (4 Refs)

254 AU - Harrison EA
AD - Natl. Technical Information Service, Springfield, VA
TI - TOXICITY OF VINYL CHLORIDE (A BIBLIOGRAPHY WITH ABSTRACTS).
SI - ICDB/79/26382
SO - Toxicity of Vinyl Chloride (A Bibliography with Abstracts). This Title Available Through National Technical Information Service, Springfield, Va., as NTIS/PS-79/0419/6GA:, NTIS/PS-79/0419, 91 pp., 1979.
LA - ENG
AB - Research is cited on the health hazards from exposure to vinyl chloride and vinyl chloride resins. Studies are included on the epidemiology of industrial and public exposures to the compound and its degradation and combustion products. (Author abstract)

255 AU - Laib RJ ; Stockle G ; Bolt HM ; Kunz W
AD - Institut fur Toxikologie, Universitat Tubingen, Wilhelmstrasse 74, D-7400 Tubingen, W. Germany
TI - VINYL CHLORIDE AND TRICHLOROETHYLENE: COMPARISON OF ALKYLATING EFFECTS OF METABOLITES AND INDUCTION OF PRENEOPLASTIC ENZYME DEFICIENCIES IN RAT LIVER.
SI - CARC/79/05816
SO - J Cancer Res Clin Oncol; 94(2):139-147 1979
LA - ENG
AB - The extent of alkylation of nucleic acid by metabolites of trichloroethylene (TCE) and vinyl chloride (VC) was compared, along with the induction, by TCE and VC, of preneoplastic foci deficient in nucleoside-5-triphosphatase in newborn Wistar rats. (1,2-14C)VC and (1,2-14C)TCE were incubated with rat liver microsomes, NADPH, and yeast RNA. TCE metabolites were irreversibly bound to proteins in microsomal incubations to a higher extent than VC metabolites, but irreversible binding to RNA was lower for TCE metabolites. Hydrolysis of the RNA that was reisolated from microsomal incubations with 14C-VC or 14C-TCE and separation of the nucleosides showed different alkylation products arising from VC and from TCE. 1,N(6)-Ethenoadenosine and 3,N(4)-ethenocytidine were produced only with metabolites of VC, possibly through the formation of an imidazol ring. The different reactivities of VC and TCE metabolites prompted a comparison of the oncogenic effects of both compounds in rat liver cells.

Newborn rats were exposed for 10 wk to 2,000 ppm VC or TCE 8 hr/day, 5 days/wk. After this period, livers of the animals were stained for nucleoside-5-triphosphatase. The VC-exposed rats showed focal hepatocellular deficiencies in this enzyme, which are supposed to represent an early sign of malignancy; no such changes were induced by TCE exposure. The data therefore suggest differences between the activity of VC and TCE in the rat liver. (24 Refs)

256 AU - Zimmerman HJ
AD - Veterans Admin. Medical Center, 50 Irving St., N.W., Washington, DC, 20422
TI - DRUG-INDUCED CHRONIC HEPATIC DISEASE.
SI - CARC/79/05660
SO - Med Clin North Am; 63(3):567-582 1979
LA - ENG
AB - The induction of chronic active hepatitis, subacute hepatic necrosis, steatosis, phospholipidosis, vascular hepatic lesions, hepatic granulomas, cirrhosis, noncirrhotic portal hypertension and neoplasms by various drugs is reviewed. The relationships between liver adenoma or carcinoma and oral contraceptives and between hepatic angiosarcoma and vinyl chloride or thorium dioxide exposure are discussed. (75 Refs)

257 AU - Daneshmend TK ; Scott GL ; Bradfield JW
AD - Bristol Royal Infirmary, Bristol BS2 8HW, England
TI - ANGIOSARCOMA OF LIVER ASSOCIATED WITH PHENELZINE.
SI - CARC/79/05635
SO - Br Med J; 1(6179):1679 1979
LA - ENG
AB - A case of liver angiosarcoma in a woman who had taken phenelzine for at least 6 yr (45 mg/day for the first 3 yr, 15 mg/day thereafter) is reported. There was no history of exposure to thorium dioxide, arsenic, or vinyl chloride. An osteolytic area suggestive of metastatic disease was present in the lateral epicondyle of the right humerus. Phenelzine administration increases the incidence of angiosarcoma in female mice, suggesting a possible etiologic relationship in this patient. (4 Refs)

258 AU - Gehring PJ ; Watanabe PG ; Park CN
AD - Toxicology Res. Lab., Dow Chemical, Midland, MI, 48640
TI - RISK OF ANGIOSARCOMA IN WORKERS EXPOSED IN VINYL CHLORIDE AS PREDICTED FROM STUDIES IN RATS.
SI - CARC/79/05599
SO - Toxicol Appl Pharmacol; 49(1):15-21 1979
LA - ENG
AB - Dose-response data for the induction of angiosarcoma in rats exposed to various levels of vinyl chloride (VC) together with attendant biotransformation data were used to estimate the risk of developing angiosarcoma in persons exposed to VC. Since a biotransformation product of VC, not VC per se, is responsible for the induction of angiosarcoma, the body surface area of

people relative to rats was used to estimate the dose of the carcinogen biotransformed from VC by the former. Four models were used to extrapolate the data. Using a probit model, 10 hepatic angiosarcomas were predicted to occur in a recently reported epidemiological cohort of 9677 workers; in actuality five have occurred. Linear models and a model based on the equation, Risk = 1-e(-betax), where x = dose, do not appear as reliable. For an 8-hr day, 5 days/week, 35-year time-weighted-average exposure of 1 ppm, the predicted incidence of hepatic angiosarcoma using the probit model is 1.5 x 10(-8). (16 Refs)

259 AU - Coustou F
AD - Univ. Bordeaux II, Bordeaux, France
TI - CARCINOGENIC RISK OF PRODUCTS USED IN THE PHARMACEUTICAL AND RELATED INDUSTRIES.
SI - CARC/79/05397
SO - IARC Sci Publ; (25):129-149 1979
LA - ENG
AB - The problems, in France, of regulating drugs to eliminate or curtail potential carcinogenicity are reviewed. Some carcinogens may be introduced during the manufacturing process, such as asbestos during filtration, vinyl chloride in aerosol production or packaging, or 2-naphthylamine and other aniline compounds during the dyeing process. The use of artificial sweeteners in the manufacture of foodstuffs is banned in France. At present, general regulations of the French government for the pharmaceutical industry state that agents should be tested for carcinogenicity prior to marketing only if: (1) the agent is closely analogous to known carcinogens or cocarcinogens; (2) a suspicion of carcinogenicity has been aroused during long-term toxicological testing; (3) the drug is to be administered over long periods of time. (22 Refs)

260 AU - Dreyon C ; Kuroki T
AD - Unit Chemical Carcinogenesis, International Agency Res. Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 2, France
TI - MUTAGENICITY OF VINYL CHLORIDE, VINYLIDENE CHLORIDE AND CHLOROPRENE IN V79 CHINESE HAMSTER CELLS.
SI - CARC/79/05341
SO - Mutat Res; 67(2):173-182 1979
LA - ENG
AB - The mutagenicity of vinyl chloride (VC), vinylidene chloride (1,1-dichloroethylene: VDC) and chloroprene (2-chloro-1,3-butadiene) was tested in V79 Chinese hamster cells in the presence of a 15,000 x g liver supernatant from phenobarbital-pretreated rats and mice. Mutations in terms of 8-azaguanine and ouabain resistance were induced in a dose-related fashion by exposure to VC vapor in the presence of the liver supernatant from phenobarbital-pretreated BDVI rats. VDC and chloroprene vapors induced a dose-related toxicity when tested with the rat liver supernatant, but these two compounds were not mutagenic in V79 cells under the assay conditions. The results are discussed with regard to the metabolic activation of

the compounds and to the correlation between the carcinogenicity of VC in humans and experimental animals. (31 Refs)

261 AU - Stockle G ; Laib RJ ; Filser JG ; Bolt HM
AD - Institut fur Toxikologie, Universitat Tubingen, Wilhelmstrasse 56, D-7400 Tubingen-1, W. Germany
TI - VINYLIDENE FLUORIDE: METABOLISM AND INDUCTION OF PRENEOPLASTIC HEPATIC FOCI IN RELATION TO VINYL CHLORIDE.
SI - CARC/79/05160
SO - Toxicol Lett; 3(6):337-342 1979
LA - ENG
AB - The tumorigenicity and metabolism of vinyl chloride (VC) and vinylidene fluoride (VF) were compared in Wistar rats. Exposure of newborn rats to VC (2,000 ppm, 8 hr/day, 5 days/wk) for 4 wk resulted in the formation of ATPase-deficient hepatocellular foci. Similar exposure to VF produced a few single foci after 10 wk. After 14 wk of exposure to VF, the number of foci was less than that observed after 4 wk of exposure to VC, and it was about 1/100 the number found after 10 wk of exposure to VC. The rate of the metabolic conversion of VF in the rat was found to be 2 orders of magnitude lower than that of VC. The very slow metabolism of VF may explain why this compound is much weaker in eliciting preneoplastic hepatic foci in newborn rats than VC. (21 Refs)

262 AU - Koizumi A ; Dobashi Y ; Tachibana Y
AD - Dept. Public Health, Faculty Medicine, Univ. Tokyo, Tokyo, Japan
TI - CHROMOSOME CHANGES INDUCED BY INDUSTRIAL CHEMICALS.
SI - CARC/79/04793
SO - Jpn J Ind Health; 21(1):3-10 1979
LA - ENG
AB - Radiation-induced chromosome damage has been widely recognized and intensively studied. Recently, attention has focused on chromosome changes induced by various industrial chemicals. In the case of occupational exposure to ionizing radiation, chromosome breaks are one of the most sensitive biological effects. Chromosome breaks have also been reported in workers exposed to benzene, vinyl chloride monomer, or styrene. Ionizing radiation, benzene, and vinyl chloride monomer are known carcinogens, and attention is now being given to carcinogenicity of clastogens or chromosome-breaking agents. Studies on in vitro chromosome breakage induced by benzene and its metabolites, as well as by cadmium, lead, and chromium compounds, are reviewed. The inhibition of repair of radiation-induced chromosome breaks by clastogens and the significance of cytogenetic studies in industrial medicine are also discussed. (40 Refs)

263 AU - Waxweiler RJ
AD - Univ. North Carolina, Chapel Hill, NC
TI - AN EPIDEMIOLOGIC INVESTIGATION OF LUNG CANCER IN A MULTIXENOBIOTIC OCCUPATIONAL ENVIRONMENT.
SI - ICDB/79/22708
SO - Diss Abstr Int (B); 39(11):5330 1979
LA - ENG
AB - An excess lung cancer risk (39 observed and 27 expected) was observed among a cohort of 4,806 males employed at a synthetic chemical plant since it opened in 1942. Upon review of the pathologic material, the excess was found to be limited to adenocarcinoma and large cell undifferentiated lung cancer. Many of the workers were exposed to vinyl chloride, but other exposures including chlorinated solvents, polyvinyl chloride (PVC) dust, acrylates, and acrylonitrile existed. Thus, detailed work histories of each cohort member along with exposure ratings of each job for each calendar yr since 1942 for each of 19 different chemicals (or chemical groups) were obtained. A serially additive expected dose model was constructed which compared the doses of the chemicals observed for the lung cancer cases to the doses expected based on subcohorts individually matched to the cases. PVC dust appeared to be the most likely etiologic agent. Observed and expected doses were then analyzed by yr before death to uncover the relevant latent period. (Author abstract) (no Refs)

264 AU - Hultmark D ; Sundh K ; Johansson L ; Arrhenius E
AD - Dept. Microbiology, Univ. Stockholm, S-106 91 Stockholm, Sweden
TI - ETHANOL INHIBITION OF VINYL CHLORIDE METABOLISM IN ISOLATED RAT HEPATOCYTES.
SI - CARC/79/04709
SO - Chem Biol Interact; 25(1):1-6 1979
LA - ENG
AB - Factors which could influence the metabolism of vinyl chloride (VC) by the liver were studied using hepatocytes and liver microsomes from untreated and phenobarbital (PB)-pretreated male strain R Wistar rats. VC incubated with hepatocytes was metabolized as a linear function of time. The metabolism was unaffected by PB pretreatment or metyrapone (40 uM), but was strongly inhibited by ethanol (4 mM) and tetrahydrofuran. Dichloro-p-nitroanisole O-demethylase was strongly stimulated in the hepatocyte preparations by PB pretreatment, and the metabolism of dichloro-p-nitroanisole was partially inhibited by metyrapone, especially after PB pretreatment. The liver microsomes showed a high capacity to convert VC to non-volatile products, this capacity being dependent on the presence of a NADPH-generating system. The microsomes were even more sensitive than the intact hepatocytes to ethanol inhibition. (20 Refs)

265 AU - Tarasova NA ; Kataeva SE
AD - Technological Inst. Meat and Dairy Industry, Moscow, USSR
TI - DETERMINATION OF VINYL CHLORIDE IN POLYMER MATERIALS, MODEL MEDIA AND FOOD PRODUCTS.
SI - CARC/79/04463
SO - Gig Sanit; (3):48-50 1979
LA - RUS
AB - Gas chromatography was used to determine vinyl chloride levels in plastic packages and bottles and in samples of cheese that were packaged in polyvinyl chloride. The use of a vapor-air phase in the chromatographic procedure increased the reliability of the assay by 3%-10%. (1 Ref)

266 AU - Harmsen H
AD - Hamburg, W. Germany
TI - VINYL CHLORIDE - ALSO A DANGER OF CANCER?
SI - ICDS/79/21002
SO - Forum Staedte Hyg; 30(3):58 1979
LA - GER
AB - The considerable progress that has been made in recent yr in the Federal Republic of Germany with respect to the control of vinyl chloride contamination of both the general environment and the immediate environment of the factories where it is processed is summarized. (3 Refs)

267 AU - Hall JA
AD - No affiliation given
TI - VINYL CHLORIDE: A HAZARD OF THE SEVENTIES.
SI - ICDS/79/20710
SO - Occup Health; 31(5):251-257 1979
LA - ENG
AB - How the hazards of vinyl chloride became known in 1974 is described and the experience of one company in dealing with the problem is related. Vinyl chloride compounds have been proven to cause angiosarcoma of the liver and osteolysis of the terminal phalanges of the fingers. The role of the occupational health nurse in dealing with such hazardous industrial compounds is stressed. (1 Ref)

268 AU - Kucerova M ; Polivkova Z ; Batora J
AD - Pediatric Dept. Postgraduate Medical Inst., Inst. Hygiene and Epidemiology, Prague, Srobarova 48, Czechoslovakia
TI - COMPARATIVE EVALUATION OF THE FREQUENCY OF CHROMOSOMAL ABERRATIONS AND THE SCE NUMBERS IN PERIPHERAL LYMPHOCYTES OF WORKERS OCCUPATIONALLY EXPOSED TO VINYL CHLORIDE MONOMER.
SI - CARC/79/04302
SO - Mutat Res; 67(1):97-100 1979
LA - ENG
AB - Three blood samples from each of nine workers occupationally exposed for 10-27 yr to vinyl chloride monomer (VCM: mean annual dose 50-20-150 ppm) were analyzed for chromosome aberrations. The third blood sample was also analyzed for sister-chromatid

exchanges (SCE's). The frequency of chromosome aberrations over a 2-yr period was nonhomogeneous, ranging from 0%-11% aberrant cells. Chromatid and chromosome breaks were detected generally; chromatid and chromosome exchanges occurred only sporadically. The SCE r frequency was more homogeneous, and it was significantly higher in the cells of VCM workers than in those of controls, ranging from 9.56 to 17.50 SCE's/cell. Smoking and other habits appeared to have no effect on the frequency of any chromosome changes. It is concluded that the routine and SCE cytogenetic analyses are equally suitable for determining high-dose VCM mutagenicity in vivo. The sensitivities of the two methods seem to be the same. (14 Refs)

269 AU - Heese B
AD - Bayerische Akademie fur Arbeits- und Sozialmedizin, Pfarrstrasse 3, 8000 Munich 22, W. Germany
TI - CHEMICALLY INDUCED OCCUPATIONAL CANCER.
SI - CARC/79/04202
SO - Munch Med Wochenschr; 97(18):837-838,855 1979
LA - GER
AB - Data on industrial chemical carcinogens are reviewed briefly. Arsenic, soot, tar, asbestos, aromatic amines, radiation, benzene, nickel, chromium-containing dust, dichlorodimethyl ether, chlorodimethyl ether, and vinyl chloride are the major industrial carcinogens. (no Refs)

270 AU - Goldschmidt BM ; Van Duuren BL ; Goldstein RC
AD - Lab. Organic Chemistry and Carcinogenesis, Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY, 10016
TI - THE REACTION OF GUANINE WITH SOME POTENTIAL METABOLITES OF 1-CHLOROPROPENE.
SI - CARC/79/03984
SO - Tetrahedron Lett; (14):1177-1180 1979
LA - ENG
AB - The bifunctional alkylating agents 2-chloropropanal and 1-chloro-1,2-epoxypropane, two potential metabolites of 1-chloropropene, were shown to react with guanine in dimethyl sulfoxide to yield the monoalkylated product 2-chloro-N-propenyl-2N-guanine. 1-Chloropropene, the simplest homolog of vinyl chloride, is carcinogenic in animals. (22 Refs)

271 AU - Guengerich FP ; Watanabe PG
AD - Dept. Biochemistry, Center Environmental Toxicology, Vanderbilt Univ. Sch. Medicine, Nashville, TN, 37232
TI - METABOLISM OF [14C]- AND [36CL]-LABELED VINYL CHLORIDE IN VIVO AND IN VITRO.
SI - CARC/79/03968
SO - Biochem Pharmacol; 28(5):589-596 1979
LA - ENG
AB - Studies were conducted to establish the roles of liver microsomal cytochrome P-450 and epoxide hydratase in the biotransformation of vinyl chloride (VC) to metabolites, particularly those bound to protein and nucleic acids. Label from [14C]VC was covalently

bound to protein and nucleic acids in vivo and in vitro in the presence of Sprague-Dawley rat liver microsomal fractions or highly purified cytochrome P-450 and NADPH-cytochrome P-450 reductase preparations. The ratio of bound to total nonvolatile metabolites increased in going from the in vivo to the microsomal to the purified system. [36C]VC was metabolized by microsomes and highly purified systems: no label was bound, and most of the metabolized chlorine could be accounted for as chloride ion. Phenobarbital pretreatment of rats did not induce total metabolism of VC in vivo at either the 10-or 250-ppm exposure levels; however, binding to protein and RNA was enhanced at the 10-ppm but not the 250-ppm level. Phenobarbital pretreatment increased the in vitro microsomal conversion of VC to both total and bound metabolites. A sizeable fraction of the label of [14C]VC metabolized in vivo was recovered in the microsomal fraction of the liver, but sodium dodecyl sulfate-polyacrylamide gel electrophoresis of in vitro incubations indicated that the metabolites were distributed among many microsomal proteins and not localized to cytochrome P-450. Evidence was obtained for the metabolism of the suspected VC metabolite chloroethylene oxide by microsomal epoxide hydratase. However, the epoxide hydratase inhibitor 3,3,3-trichloropropylene oxide, which blocks the microsomal degradation of chloroethylene oxide, did not enhance the level of VC bound to either protein or adenosine. (39 Refs)

272 AU - Magnusson J ; Hallstrom I ; Ramel C
AD - Environmental Toxicology Unit, Wallenberg Lab., Univ. Stockholm, S-106 91 Stockholm, Sweden
TI - STUDIES ON METABOLIC ACTIVATION OF VINYL CHLORIDE IN DROSOPHILA MELANOGASTER AFTER PRETREATMENT WITH PHENOBARBITAL AND POLYCHLORINATED BIPHENYLS.
SI - CARC/79/03961
SO - Chem Biol Interact; 24(3):287-298 1979
LA - ENG
AB - The metabolic activation of vinyl chloride (VC) by the hepatic mixed-function oxygenase system was studied in Drosophila melanogaster by measuring the uptake of 14C from labeled VC in five different strains with and without pretreatment with phenobarbital or a polychlorinated biphenyl (PCB: Clophen A50). The latter compounds are well-known inducers of cytochrome P-450. In accordance with previous data on VC-induced sex-linked recessive lethals, pretreatment with inducers increased the uptake of labeled compound up to 10 times. There was, however, a marked difference in response among the five strains. In particular, the Hikone strain, known to be resistant to insecticides, had a comparatively higher initial uptake of VC than any of the other strains tested. However, this uptake was unaffected by phenobarbital, even at doses 10 times higher than those used with the other strains, and it was induced to only a very small degree by PCB. Crosses between Hikone and an inducible strain indicated essentially a dominance for the Hikone genotype. Tests of inducible strains showed the same response to phenobarbital by 2 hr old larvae and adult males and females. The

use of dimethyl sulfoxide as a solvent decreased both the initial uptake of 14C and, particularly, the induction by PCB. The use of Tween 80 as an emulsifier did not have such an effect. The interstrain variation in metabolic activation and inducibility has to be considered for optimization of the use of Drosophila in mutagenicity testing. This variation also opens up new possibilities of analyzing the mixed-function oxygenase system biochemically and genetically. (26 Refs)

273 AU - Rannug U ; Beije B
AD - Division Toxicology Genetics, Wallenburg Lab., Univ. Stockholm, Stockholm, Sweden
TI - THE MUTAGENIC EFFECT OF 1,2-DICHLOROETHANE ON SALMONELLA TYPHIMURIUM. II. ACTIVATION BY THE ISOLATED PERFUSED RAT LIVER.
SI - CARC/79/03960
SO - Chem Biol Interact; 24(3):265-285 1979
LA - ENG
AB - Isolated Wistar rat liver was perfused with a soln containing 1,2-dichloroethane (DCE), 1,2-dibromoethane (DBE), or 2-chloroethanol (CE), and the mutagenicities of the perfusates for Salmonella typhimurium strains TA1530 and TA1535 were tested. Bile samples (diluted 10-fold) produced by DCE-treated livers were strongly mutagenic for TA1535, the greatest values (800 and 600 mutants/plate) being observed 15 or 30 min after addition of DCE (360 micromoles (mumol)) at 0 and 90 min, respectively. Bile from DBE-treated livers (1 dose of 12 mumol DBE) was also mutagenic for TA1535, producing 50 and 60 mutants/plate at 15 and 30 min, respectively. Bile from DCE-treated Sprague-Dawley rats was significantly less mutagenic than that of Wistar rat bile (p less than 0.001), and the former was clearly more mutagenic after 30 min than after 15 min. CE was not mutagenic in this system. The results with DCE and DBE indicated an activation through conjugation to glutathione with a subsequent excretion through the bile. Bile produced by mice treated ip with DCE (80 mg/kg) was also mutagenic for TA1535, the mutagenicity being greater 30 min after injection than 60 min after injection. S-(2-chloroethyl)-L-cysteine and N-acetyl-S-(2-chloroethyl)-L-cysteine were equally mutagenic for TA1535 in the concentration range 0.2-0.6 mumol/plate, whereas S-(2-hydroxyethyl)-L-cysteine was not directly mutagenic. Differences and similarities in the metabolism of DCE and vinyl chloride are discussed on the basis of these results. (49 Refs)

274 AU - Stellman JM
AD - Div. Occupational Health and Toxicology, American Health Foundation, New York, NY
TI - THE EFFECTS OF TOXIC AGENTS ON REPRODUCTION.
SI - CARC/79/03935
SO - Occup Health Saf; 48(3):36-43 1979
LA - ENG
AB - Aspects of the toxicology of human reproduction are reviewed, with particular emphasis on the effects of toxic agents encountered in the workplace. Potential modes of reproductive

dysfunction include organ dysfunction, genetic defects, gestational effects, and postpartum effects. Substances that may affect reproduction include diethylstilbestrol (DES), estrogen, thalidomide, anesthetic gases, vinyl chloride, chloroprene, dibromochloropropane, DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane), copper in intrauterine devices), lead, and nonionizing radiation. (no Refs)

275 AU - Tamburro CH ; Creech JL ; Greenberg RA ; Makk L ; Whelan JG
AD - Cancer Center, Div. Digestive Diseases and Nutrition, Univ. Louisville, Sch. Medicine, Louisville, KY
TI - MEDICAL SURVEILLANCE SYSTEM FOR NEOPLASTIC AND NON-NEOPLASTIC OCCUPATIONAL INJURIES DUE TO INDUSTRIAL CHEMICALS (MEETING ABSTRACT).
SI - ICDB/79/17714
SO - Clin Res; 27(2):285A 1979
LA - ENG
AB - Following the discovery of a rare liver cancer (angiosarcoma) among vinyl chloride polymerization workers in 1974, a prospective medical surveillance program was designed for the early subclinical detection of occupational injuries, including neoplasia. This prototype program involved the active cooperation of a local hospital, a regional university cancer center, the plant workers, labor leaders, management and regulatory agencies. In the first 4 yr of operation, this program identified an increased incidence of hepatic angiosarcoma among vinyl chloride workers, as well as an increased occurrence of such non-neoplastic, and possibly pre-malignant, lesions as peliosis hepatis, portal fibrosis, portal hypertension, splenomegaly and mid-zonal pleural fibrous thickening of lung. A systematic multi-disciplinary evaluation system was developed to determine if the diseases and disorders detected could be related to occupational chemical exposure. This program identified the job-related nature of hepatic angiosarcoma and its causative agent from among 22 different chemicals via individual chemical exposure histories based on a retrospective rank-order system for the various job classifications. This medical health surveillance system can be applied in any industry effectively without significant interference in workers' life or industrial function, at a cost effective level (av cost less than 5,000 dollars/yr/1000 workers provided that all participating parties actively cooperate. (no Refs)

276 AU - Telles NC ; Thomas LB ; Popper H ; Ishak KG ; Falk H
AD - Bureau Radiological Health, Food and Drug Admin., Rockville, MD, 20857
TI - EVOLUTION OF THOROTPAST-INDUCED HEPATIC ANGIOSARCOMAS.
SI - CARC/79/03722
SO - Environ Res; 18(1):74-87 1979
LA - ENG
AB - Pathological findings in 25 cases of Thorotrast-induced angiosarcoma are presented. Characteristic antecedent or precursor changes similar to previously described changes present

in hepatic angiosarcoma secondary to vinyl chloride, or arsenicals or of unknown etiology were found. The antecedent or precursor change consisted of areas with simultaneous activation of both the hepatocytes and sinusoidal cells and associated lesions in the sinusoidal and perisinusoidal spaces. The hepatic cell plates surrounding these areas were compressed, with subsequent development of fibrous septa at the interface between the areas of mixed hyperplasia and the areas of compression. In these multiple areas, multicentric angiosarcomas developed in close approximation to the portal tracts but not to the Thorotrast deposits. (24 Refs)

277 AU - Falk H ; Telles NC ; Ishak KG ; Thomas LB ; Popper H
AD - Chronic Diseases Div., Bureau Epidemiology, Center Disease Control, US Dept. Health, Education and Welfare, Public Health Service, Atlanta, GA, 30333
TI - EPIDEMIOLOGY OF THOROTRAST-INDUCED HEPATIC ANGIOSARCOMA IN THE UNITED STATES.
SI - CARC/79/03714
SO - Environ Res; 18(1):65-73 1979
LA - ENG
AB - Twenty-six cases of Thorotrast (TT)-induced hepatic angiosarcoma (HAS) were identified in an epidemiologic investigation of HAS's occurring in the US during 1964-1974. TT was administered to the 26 patients (19 men, 7 women) during 1931-1953, with 68% of the patients being injected in the 1940's. The mean age at the time of exposure was 28.5 yr, and the mean age at death was 54.5 yr. Indications for TT studies were carotid arteriography (14 cases), hepatolienography (9), femoral arteriography (2), and phlebography (1). Information on the TT dose administered was available for 14 patients, 9 of whom a mean dose of 39.9 ml for carotid angiography, 4 a mean dose of 61.8 ml for hepatolienography, and 1 a dose of 10-20 ml for a femoral arteriogram. Four patients had a history of preexisting liver disease, two had hemolytic anemia, and one had arteriovenous malformations. None of the patients had a history of exposure to vinyl chloride, but two had been exposed to arsenic and two to iron dust. An additional two patients were chronic alcoholics. These additional risk factors may have potentiated the effects of TT. (35 Refs)

278 AU - Woods JS
AD - Battelle Human Affairs Res. Centers, 4000 N. E. 41st St., Seattle, WA, 98105
TI - EPIDEMIOLOGIC CONSIDERATIONS IN THE DESIGN OF TOXICOLOGIC STUDIES: AN APPROACH TO RISK ASSESSMENT IN HUMANS.
SI - CARC/79/03585
SO - Fed Proc; 38(5):1891-1896 1979
LA - ENG
AB - A six-step procedure for including epidemiologic considerations in the design and analysis of laboratory studies designed to estimate risk of toxicity in humans during low-level exposure to environmental chemicals is described. Epidemiologic data are

first used to identify the incidence of toxicity associated with high-level exposure of humans to a particular agent. This information is used to design chronic toxicity studies in animals that establish a dose-response relationship for that substance. Clinical, epidemiologic, and laboratory research data are then used to adjust for differences in major biological determinants of responsiveness between test animals and humans, and biostatistical procedures are used to describe the nature of the dose-response relationship in the low-dose region where community exposure occurs. Human incidence of toxicity under prevailing environmental conditions is then estimated from the adjusted animal model. Finally, epidemiologic studies are conducted to confirm (or deny) the validity of the predictive model. Vinyl chloride (VC)-induced hepatic angiosarcoma is used show to how epidemiologic data might be useful in the experimental assessment of toxicity risk in human populations. Despite numerous uncertainties and assumptions inherent in the procedure, the VC example suggests the importance of a combined epidemiologic-toxicologic approach to risk assessment in humans and to setting exposure limitations for toxic agents in the environment. (30 Refs)

279 AU - Ottenwalder H ; Laib RJ ; Bolt HM
AD - Institut fur Toxikologie, Universitat Tubingen, Wilhelmstrasse 56, D-7400 Tubingen-1, W. Germany
TI - ALKYLATION OF RNA BY VINYL BROMIDE METABOLITES IN VITRO AND IN VIVO.
SI - ICDB/79/16345
SO - Arch Toxicol (Berl); 41(4):279-286 1979
LA - ENG
AB - The compound (1,2-14C)vinyl bromide was incubated with rat liver microsomes, NADPH, and polyadenylic acid, polycytidylic acid, or RNA, respectively. Part of the adenosine moieties in RNA or in polyadenylic acid were alkylated and labeled 1,N(6)-ethenoadenosine structures were formed. Part of the cytidine moieties were converted into 3,N(4)-ethenocytidine. In addition, a further unidentified cytidine alkylation product was observed which was not seen in experiments using (1,2-14C)vinyl chloride. When rats were exposed to (1,2-14C)vinyl bromide, radioactive ethenoadenosine and ethenocytidine were present in hydrolysates of liver RNA. A further alkylation product was observed in the RNA hydrolysates which did not occur in experiments using (14C)vinyl chloride. The data show that vinyl bromide metabolites alkylate nucleic acids; although in general in this respect vinyl bromide and vinyl chloride behave similarly, some differences are observed in the alkylation behavior of both compounds. (Author abstract) (14 Refs)

280 AU - Bartsch H ; Malaveille C ; Barbin A ; Planche G
AD - International Agency for Res. Cancer, 150 Cours Albert-Thomas, F-69372 Lyon, Cedex 2, France
TI - MUTAGENIC AND ALKYLATING METABOLITES OF HALO-ETHYLENES, CHLOROBUTADIENES AND DICHLOROBUTENES PRODUCED BY RODENT OR HUMAN LIVER TISSUES. EVIDENCE FOR OXIRANE FORMATION BY P450-LINKED MICROSOMAL MONO-OXYGENASES.
SI - CARC/79/03420
SO - Arch Toxicol (Berl); 41(4):249-277 1979
LA - ENG
AB - The abilities of various haloolefins to induce his+ revertants in Salmonella typhimurium strains TA100 and TA1530 in the presence of mouse or human postmitochondrial liver supernatants were studied. With mouse liver microsomes, mutagenicity decreased in the following order: 3,4-dichlorobutene-1 greater than 1-chlorobutadiene greater than 2-chlorobutadiene greater than vinyl bromide greater than vinylidine chloride (VDC) greater than vinyl chloride (VC). 1,1,2-Trichloroethylene and 1,1-difluoroethylene were marginally mutagenic, and tetrachloroethylene and vinyl acetate were nonmutagenic. With human liver fractions, VC, vinyl bromide, VDC, and 2-chlorobutadiene were mutagenic. 1,4-Dichloro-2,3-epoxybutane was less mutagenic than 1,4-dichlorobutene-2, the mutagenicity of which was increased by liver microsomes. The mutagenicities of VC and VDC were increased up to twofold in the presence of liver microsomes from rats pretreated with phenobarbital or 3-methylcholanthrene, but pregnenolone-16alpha-carbonitrile, aminoacetonitrile, disulfiram pretreatment decreased the mutagenic effects. VC and, probably, vinyl bromide were epoxidized by mouse liver microsomes. 2-Chlorobutadiene, but not 1,1-difluoroethylene, 1,1-dichloroethylene, or 1,1,2-trichloroethylene, yielded an alkylating intermediate. The alkylating activity of 2-chloro- and 1-chlorobutadiene, 3,4-dichlorobutene-1, and 1,4-dichlorobutene-2 and its 2,3-epoxide derivative was not related quantitatively to mutagenicity. The data indicate that oxidation of the double bond in certain haloolefins is a common pathway in the formation of biologically active intermediates. (78 Refs)

281 AU - Bahlman LJ ; Alexander V ; Infante PF ; Wagoner JK ; Lane JM
AU - Bingham E
AD - Natl. Inst. Occupational Safety and Health, 5600 Fishers Lane, Rockville, MD, 20857
TI - VINYL HALIDES: CARCINOGENICITY. VINYL BROMIDE, VINYL CHLORIDE, AND VINYLIDENE CHLORIDE.
SI - CARC/79/03415
SO - Am Ind Hyg Assoc J; 40(4):A-30-A-40 1979
LA - ENG
AB - Laboratory studies demonstrating the carcinogenicity and mutagenicity of vinyl chloride (VC), vinylidine chloride (VDC), and vinyl bromide (VB) are reviewed, together with studies demonstrating the carcinogenicity and mutagenicity of VC in

humans. Liver angiosarcomas have been induced in rats or mice by vinyl halide concentrations of 25-55 ppm. It is recommended that VB and VDC be considered in the workplace as potential carcinogens to humans and controlled with the same degree of prudence as VC. (35 Refs)

282 AU - Diubankova EN ; Bykhovskii AV
AD - F. F. Erisman Res. Inst. Hygiene, Moscow, USSR
TI - HAZARDS ASSOCIATED WITH EXPOSURE TO VINYL CHLORIDE AND POLYVINYL CHLORIDE MATERIALS.
SI - CARC/79/03204
SO - Gig Sanit; (1):69-74 1979
LA - RUS
AB - Current data on the hazards of vinyl chloride (VC), in general, and of the use of polyvinyl chloride packages, in particular, are reviewed. Seventeen cases of liver angiosarcoma have been reported in workers in the VC industry (compared with the total 45 cases reported in the world literature). In addition to liver angiosarcomas, the workers had an increased incidence of cancer of the respiratory, CNS, lymph, and hematopoietic systems. The long-term storage of alcohol in PVC bottles showed distinct organoleptic changes in the alcohol that prompted a ban on the use of PVC containers for food products containing alcohol. (26 Refs)

283 AU - Buffler PA ; Wood S ; Eifler C ; Suarez L ; Kilian DJ
AD - Univ. Texas Sch. Public Health, P. O. Box 20186, Houston, TX, 77025
TI - MORTALITY EXPERIENCE OF WORKERS IN A VINYL CHLORIDE MONOMER PRODUCTION PLANT.
SI - CARC/79/03199
SO - J Occup Med; 21(3):195-203 1979
LA - ENG
AB - A mortality follow-up study was conducted of 464 white men employed in a vinyl chloride monomer (VCM) production plant for at least two consecutive mo between 1948 and 1975. Eight of the 28 deaths in this group were due to malignant neoplasms, 4 from lung cancer. No angiosarcomas or other liver tumors were observed. The eight persons who died of cancer were initially exposed to VCM prior to 1963, and the four with lung cancer, prior to 1958. Six of the 28 deaths, including 2/8 cancer deaths, occurred among a subgroup of 165 workers exposed to 1,4-dioxane. The total number of observed cancer deaths was not significantly different than that expected, but a significant excess was noted for malignant neoplasms of the respiratory system. The effects of smoking, duration of exposure to VCM, and level of exposure and the combined effect of duration and level of exposure were analyzed separately. A 5 yr latency requirement was maintained for all analyses except for the smoking analysis. Using a minimum latency period of 5 yr from the date of initial exposure to VCM, the excess of respiratory cancer was moderate but not significant for the 314 employees satisfying this criterion. Both a longer duration and a higher level of exposure during the first 5 yr

were associated with a signficant excess of respiratory cancer. However when duration and level of exposure were combined, the results were not significant. In spite of the discrepancy in the results of dose-response analyses, the results suggest that a relationship exists between exposure to VCM and respiratory cancer. (27 Refs)

284 AU - Fortwengler HP ; Jones D ; Tamburro CH ; Espinosa E
AD - Univ. Louisville Sch. Medicine, Louisville, KY, 40232
TI - FACTOR VIII CONTENT AS EVIDENCE FOR ENDOTHELIAL ORIGIN OF VINYL CHLORIDE ASSOCIATED LIVER ANGIOSARCOMA (MEETING ABSTRACT).
SI - ICDB/79/14739
SO - Fed Proc; 38(3,part2):999 1979
LA - ENG
AB - To ascertain the endothelial cell origin of VCA we have looked for Factor VIII in the tumor since this factor appears to be specific for such cells. Frozen sections of three VCA and one idiopathic case were examined for presence of Factor VIII by indirect immunofluorescence. Sections of angiosarcoma demonstrated a strikingly increased specific fluorescence which lined enlarged sinusoids. This intense fluorescence was easily seen on a low power (100x) as an irregular or splotchy pattern. Occasional striations of linear fluorescence which did not follow hepatic cords were also present. A similar pattern of staining was also given by the idiopathic angiosarcoma but was never seen in sinusoids of normal liver. These observations were further supported by the finding that absorption of Factor VIII antiserum with experimental angiosarcoma tissue resulted in complete inhibition of immunofluorescence. These findings demonstrate that VCA and idiopathic angiosarcoma include proliferating cells containing Factor VIII and therefore strongly support an endothelial cell origin of this tumor. (1 Ref)

285 AU - Goldschmidt BM ; Van Duuren BL ; Goldstein PC ; Smith AC
AD - Lab. Organic Chemistry, Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY, 10016
TI - CARCINOGENICITY AND CHEMICAL REACTION WITH GUANINE OF 1-CHLOROPROPENE AND TWO OF ITS POTENTIAL METABOLITES (MEETING ABSTRACT).
SI - ICDB/79/13857
SO - Proc Am Assoc Cancer Res; 20:90 1979
LA - ENG
AB - 1-Chloropropene, the simplest homologue of the human carcinogen vinyl chloride, along with two of its potential metabolites, 1-chloro-1,2-epoxypropane and 2-chloropropanal, were tested for carcinogenicity in female ICR/Ha Swiss mice (30/group). Repeated skin application of the alkene or aldehyde, and single dose initiation of the three compounds followed by promotion with phorbol myristate acetate failed to yield skin tumors. However, weekly sc injection of the aldehyde (1.0 mg) yielded 4 local sarcomas (P less than 0.005). Weekly intragastric feeding of the alkene (1.0 mg) led to 10 forestomach papillomas and 3 carcinomas (P less than 0.0005) while the aldehyde (1.0 mg) led to 6

forestomach papillomas (P less than 0.05). Upon being allowed to react with guanine in dimethylsulfoxide the alkene failed to react, while the epoxide and aldehyde yielded the identical new compound, C8H8ClN5O. Based on UV and nuclear magnetic resonance spectra and other data the structure of the compound was established. It is an enamine formed by reaction at the 2-amino group of guanine. It should be noted that the potent carcinogenic metabolites of benzo(a)pyrene react predominantly with the 2-amino group of guanine in polynucleotides, just as the potential metabolites of 1-chloropropene did in our study. (no Refs)

286 AU - Lande SS
AD - Center Chemical Hazard Assessment, Syracuse Res. Corporation, Merrill Lane, Syracuse, NY, 13210
TI - MEASUREMENT OF ATMOSPHERIC VINYL CHLORIDE.
SI - ICDB/79/13784
SO - Am Ind Hyg Assoc J; 40(2):96-107 1979
LA - ENG
AB - Vinyl chloride atmospheric assays were reviewed for lowest detection limits and most specific measurements. Vinyl chloride is widely used, especially for polyvinyl chloride production, an is a potent carcinogen known to cause hepatic angiosarcoma. Gas chromatography of a sample adsorbed on charcoal is apparently th most sensitive and reliable method. (41 Refs)

287 AU - Dannaher C ; Yam LT ; Tamburro C
AD - Div. Hematology-Oncology and Vinyl Chloride Project, Univ. Louisville, Louisville, KY, 40202
TI - VINYL CHLORIDE ASSOCIATED HEPATIC ANGIOSARCOMA CHEMOTHERAPY (MEETING ABSTRACT).
SI - ICDB/79/13247
SO - Proc Am Assoc Cancer Res; 20:358 1979
LA - ENG
AB - Hepatic angiosarcoma is a rare tumor probably arising from the vascular lining cells. Industrial exposure to vinyl chloride used in plastics production has been found to be associated with a 400-fold increase of tumor incidence over that expected in the general populatiodn. By the time of diagnosis, the tumor is usually diffusely spread throughout the liver and surgery or radiation therapy are not treatment alternatives. Mean duration of survival of untreated patients is 6 mo. We have investigated the use of systemic chemotherapy in a group of workers with hepatic angiosarcoma from a local industry using vinyl chloride. Five patients with histological diagnosis were studied. All of the patients received adriamycin 60 mg/square meter (m2) iv every 3-4 wk. In four patients this was combined with cytoxan 600 mg/m2 and methotrexate 20 mg/m2. Mild thrombocytopenia and/or granulocytopenia was the rule with each treatment course. One patient developed sepsis during a period of granulocytopenia. No patient died due to complications of chemotherapy. Response criteria included significant change in liver size, tumor size, liver function test and performance status lasting at least 2 mo.

Three patients had an objective response lasting 4, 9 and 48+ mo. One patient had stable disease for 10 mo. and the fifth patient had progressive disease. Responding patients maintained an excellent performance status during therapy. Following evidence of no response or progressive disease, patients expired in 2, 3, 4, and 6 mo, respectively. Survival from time of diagnosis was 4, 11, 13, 15 and 48+ mo. Sufficient data are not available from these patients to recommend a specific drug or combination for use in hepatic angiosarcoma, but our data indicate that chemotherapy can improve quality and duration of survival. (no Refs)

288 AU - Fishbein L
AD - National Center Toxicological Res., Jefferson, AR, 72079
TI - POTENTIAL HALOGENATED INDUSTRIAL CARCINOGENIC AND MUTAGENIC CHEMICALS. I. HALOGENATED UNSATURATED HYDROCARBONS.
SI - CARC/79/02961
SO - Sci Total Environ; 11(2):111-161 1979
LA - ENG
AB - Data on the carcinogenicity and mutagenicity of several of the most industrially significant halogenated unsaturated hydrocarbons are reviewed to assess the nature of their present potential risk. These compounds are vinyl chloride, vinylidine chloride, trichloroethylene, perchloroethylene, chloroprene, trans-1,4-dichlorobutene, hexachlorobutadiene, and allyl chloride. Aspects of their synthesis (primarily in terms of the nature of possible hazardous trace impurities), production volumes and use patterns, chemical and biological reactivity and stability, environmental occurrence, and national permissible worker exposure levels are considered. Experimental and human epidemiologic evidence of the carcinogenicity and mutagenicity of the hydrocarbons is reviewed, as are data concerning their in vivo and in vitro metabolism. (302 Refs)

289 AU - Renga G
AD - Istituto di Igiene, Universita degli Studi di Ancona, Ancona, Italy
TI - BRONCHOPULMONARY TUMORS: EPIDEMIOLOGY.
SI - CARC/79/02706
SO - Minerva Med; 70(3):173-194 1979
LA - ITA
AB - Epidemiological and etiological data on lung cancer are reviewed. In Europe, lung cancer mortality is greater than 100/100,000 in England; 61-99/100,000 in Germany, Switzerland, Austria, Denmark, Netherlands, Belgium, and Finland; 31-60/100,000 in Poland, Bulgaria, Greece, Hungary, Italy, France, Ireland, and Sweden; and 16-30/100,000 in Yugoslavia, Spain, Portugal, Romania, Norway, and Iceland. In Italy, a positive correlation was found between the size of a city in terms of population and lung cancer mortality. Air pollution, occupational exposure to harmful substances, and smoking are considered the principal environmental factors of lung cancer. Industrial pollutants suspected of inducing lung cancer in humans include uranium,

radon, hematite, polycyclic aromatic hydrocarbons, asbestos, arsenic, chromium, nickel, mustard gas, acrylonitrile, chloromethyl ether, and, possibly, beryllium and vinyl chloride. Carcinogens detected in tobacco smoke include dimethylnitrosamine, diethylnitrosamine, methylethylnitrosamine, N-nitrosopyrrolidine, nitrosopiperidine, benzo(a)pyrene, methylbenzo(a)pyrene, dibenzoacridine, dibenzocarbazole, beta-naphthylamine, benzofluoranthene, methylfluoranthene, benzanthracene, chrysene, nitrosoanabasine, benzophenanthrene, nitrosonornicotine, polonium-210, and arsenic. (55 Refs)

290 AU - Chen KT ; Bolles JC ; Gilbert EF
AD - Dept. Pathology, Univ. Wisconsin Center for Health Sciences, Madison, WI
TI - AGIOSARCOMA OF THE SPLEEN.
SI - ICDB/79/10470
SO - Arch Pathol Lab Med; 103(3):122-124 1979
LA - ENG
AB - Results of the ultrastructural study of one of two cases of splenic angiosarcoma established the blood vessel origin of this tumor. Fifty-three previously reported cases were reviewed. None of the 55 patients had a history of exposure to thorium dioxide, vinyl chloride, or arsenic, which are known to be associated with hepatic angiosarcoma and other tumors. A comparison of the splenic and hepatic angiosarcomas showed that tumors not associated with exogenous material frequently involve the spleen and liver simultaneously, and that tumors associated with thorium dioxide, vinyl chloride, or arsenic commonly involve the liver with sparing of the spleen. (Author abstract) (29 Refs)

291 AU - Zuccato E ; Marcucci F ; Fanelli R ; Mussini E
AD - Istituto di Richerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milan, Italy
TI - HEAD-SPACE GAS-CHROMATOGRAPHIC ANALYSIS OF VINYL CHLORIDE MONOMER IN RAT BLOOD AND TISSUES.
SI - CARC/79/02455
SO - Xenobiotica; 9(1):27-31 1979
LA - ENG
AB - Vinyl chloride monomer (VCM) levels in rat blood and tissues were measured by a head-space gas chromatograph fitted with a flame ionization detector. Male CD rats were given VCM (1, 5, or 10 mg/kg iv or 10 mg/kg po) and killed 1-120 min later. VCM deposition was determined in blood, liver, kidney, brain, and lung. VCM was distributed rapidly after iv administration; blood had the highest concentration at 1 min, but brain and kidney levels attained equilibrium with blood levels within 2 min of injection. VCM in both blood and tissues was no longer detectable at 15 min for the highest iv dose and at 4 min for the lowest. VCM concentrations were lower in the lung than in blood and other organs at all times. Liver concentrations were generally lower than those of brain and kidney. VCM reached a high concentration in blood at 5 min after po administration, indicating rapid absorption from the gastrointestinal tract. At 60 min it was

detectable only in traces, and at 120 min it was no longer detectable. VCM concentrations in the liver were higher than those in blood up to 20 min, but they decreased faster than those in the other tissues, suggesting that metabolism by the liver may determine the disposition of VCM. The technique described is sensitive to 5 nanograms (ng)/ml VCM in blood and 30 ng/g in tissues. (15 Refs)

292 AU - Department of Labor
AD - Occupational Safety and Health Admin., Dept. Labor, Washington, DC
TI - OCCUPATIONAL SAFETY AND HEALTH STANDARDS: TOXIC AND HAZARDOUS SUBSTANCES.
SI - ICDB/79/09801
SO - Fed Regist; 44(29,Book2):8575-8833 1979
LA - ENG
AB - Occupational safety and health standards for toxic and hazardous substances which are applicable to construction are presented. The substances discussed include asbestos, coal tar pitch volatiles, 4-nitrobiphenyl, alpha-naphthylamine, methyl chloroethyl ether, 3,3-dichlorobenzidine and its salts, bis-chloromethyl ether, beta-naphthylamine, benzidine, 4-aminodiphenyl, ethyleneimine, beta-propriolactone, 2-acetylaminofluorene, 4-dimethylaminoazobenzene, N-nitrosodimethylamine, vinyl chloride, inorganic arsenic, benzene, coke oven emissions, cotton dust (in cotton gins), 1,2-dibromo-3-chloropropane, and acrylonitrile. (no Refs)

293 AU - Hooper NK ; Harris RH ; Ames BN ; Schneiderman MA
AD - Dept. Biochemistry, Univ. California, Berkeley, CA, 94720
TI - CHEMICAL CARCINOGENS (LETTER TO EDITOR).
SI - CARC/79/02197
SO - Science; 203(4381):602-603 1979
LA - ENG
AB - Two studies cited in a recent report on chemical carcinogens that support the threshold theory, one concerning vinyl chloride and one concerning chloroform, are criticized. The basic arguments that detoxifying mechanisms are overwhelmed at high dose levels and that high doses of chemicals cause pathological damage to tissues and increase their susceptibility to cancer are countered by other studies showing the opposite results. In addition, a biological model implied in the report--that logarithm of the percent of animals developing a tumor is linearly related to the logarithm of the dose--is inappropriate. (16 Refs)

294 AU - Locker GY ; Doroshow JH ; Zwelling LA ; Chabner BA
AD - Clinical Pharmacology Branch, NCI, Bldg. 10, Room 6N119, 9000 Rockville Pike, Bethesda, MD, 20014
TI - THE CLINICAL FEATURES OF HEPATIC ANGIOSARCOMA: A REPORT OF FOUR CASES AND A REVIEW OF THE ENGLISH LITERATURE.
SI - CARC/79/02132
SO - Medicine (Baltimore); 58(1):48-64 1979
LA - ENG
AB - The clinical features and treatment of hepatic angiosarcoma are

discussed based on four case reports and a review of 99 cases from the English literature. An apparent etiology was identified in 43/103 cases: vinyl chloride in 22, thorotrast in 15, arsenicals in 2, radium in 1, and underlying hemochromatosis in 3. The tumor was most common in middle-aged men. The most common symptoms were abdominal pain, weakness, fatigue, and wt loss, and the most common presenting physical findings were hepatomegaly, ascites, and jaundice. Abnormalities in liver function tests, thrombocytopenia, and elevated prothrombin time were frequent laboratory findings. Arteriography was a valuable diagnostic tool, as was open biopsy at surgery. However, liver biopsy was accompanied by both morbidity and mortality, especially related to bleeding. Problems encountered during the clinical course included hepatic failure, intraabdominal and gastrointestinal bleeding, and peripheral destruction of blood elements. The median survival time from the first symptom was 5.5 mo, and only 3% of the patients lived greater than 2 yr. (144 Refs)

295 AU - Turns D ; Stevenson J
AD - No affiliation given
TI - HEALTH EDUCATION AND WORK MISTRUST IN A CANCER PREVENTION PROJECT.
SI - ICDB/80/52849
SO - UICC Tech Rep Ser; 31:47-52 1978
LA - ENG
AB - A random sample of 121 workers at the B F Goodrich 4 Chemical Company in Louisville, Kentucky participated in an opinion survey aimed at assessing the prevalence of negative feelings among workers toward a comprehensive medical surveillance program instituted for the workers who had been exposed to vinyl chloride. About 21% of the employees felt that the health questions that they had asked had not been properly answered, 12% believed that the physicians were out to protect the company, 10% expressed concern about a breach of confidentiality, and 30% felt that the company had done the most (compared with unions, government agencies, etc) to protect the employees from the hazards of vinyl chloride. It was concluded that the program was well accepted by the employees. (5 Refs)

296 AU - Cicek J
AD - No affiliation given
TI - POTENTIAL SIGNIFICANCE OF SOME ASPECTS OF MODERN VINYL CHLORIDE TECHNOLOGY ON THE GENESIS OF HEPATIC DISEASE.
SI - ICDB/80/48251
SO - Libri Oncol; 7(3/4):227-232 1978
LA - SCR
AB - Studies of the effects of vinyl chloride on the development of hepatic disease are reviewed. Occupational exposure to vinyl chloride may result in angiosarcoma of the liver, and polyvinyl chloride may contain 5-1,000 ppm of vinyl chloride. (44 Refs)

297 AU - Preussmann R
AD - Institut Toxikologie und Chemotherapie, Deutsches Krebsforschungszentrum, D-6900 Heidelberg 1, W. Germany
TI - TOXICOLOGICAL ASPECTS OF FOOD SAFETY - CARCINOGENICITY AND MUTAGENICITY.
SI - ICOB/80/46077
SO - Arch Toxicol Suppl; (1):69-84 1978
LA - ENG
AB - One major problem in the evaluation of potential carcinogenic food additives and contaminants is that of thresholds or, better, of 'no adverse-effect-levels'. Arguments in favor of the postulated 'irreversibility' of carcinogenic effects are based on dose-response studies, single-dose and multi-generation experiments as well as on the concept of somatic mutation as the first steps in carcinogenesis with subsequent transmittance of induced defects during cell replication. The problem of extrapolation of results of animal experiments using high doses of low exposure and low incidences in man is not yet solved satisfactorily. Possible practical consequences include zero-tolerance, acceptable thresholds at low risk and safety factors. Acceptable intakes never should be considered constants but should be changeable as soon as new facts in regard to the safety evaluation are available. Several systems of short-term tests as screening methods are based on mutagenicity tests and offer many advantages. Their critical evaluation is of utmost importance. Examples of some relevant problems to be discussed include nitrosamines in food products and their formation from ingested precursors; the migration of vinyl chloride from polyvinyl chloride food packing material; the occurrence of low levels of chloroform in drinking water. (Author abstract) (60 Refs)

298 AU - Lambotte-Vandepaer M ; Noel G ; Rollmann B ; Mercier M
AU - Roberfroid M
AD - Lab. Biotoxicology, Catholic Univ. Louvain, Sch. Pharmacy, UCL 73.69, Avenue Emm. Mounier 73, B-1200 Bruxelles, Belgium
TI - MODIFYING EFFECTS OF STYRENE ON THE CATALYTIC PROPERTIES OF SOME MICROSOMAL ENZYMES.
SI - ICOB/80/46071
SO - Arch Toxicol (Berl); (1):287-290 1978
LA - ENG
AB - The recent concern with the carcinogenic and/or the mutagenic effects of vinyl chloride has focused attention to the potential hazards of a large variety of monomers used in the manufacture of various plastic materials. The structural relationship between styrene (vinyl benzene) and vinyl chloride, as well as the frequency of human exposure to styrene, prompted us to carefully investigate some of the effects of styrene on some microsomal enzymes, the role of the which is essential in activation and deactivation processes of most chemical carcinogens. We have recently demonstrated that pretreatment of rats with different carcinogens selectively increases the affinity of the activating

enzymes towards their own substrates, thereby favoring the production of the active carcinogenic intermediate. In the present experiment, adult male rats have been treated with various doses of styrene, administered either ip or by inhalation. The activities of some microsomal enzymes, such as aryl hydrocarbon hydroxylase, cytochrome P 450, NADPH: cytochrome c reductase, styrene oxidase hydratase and aldrin oxidase were measured. Some of the treatments have been shown to significantly modify the catalytic properties of the enzymatic systems more or less directly implicated in the metabolic transformations of styrene into its mutagenic intermediate: styrene oxide and of this latter one, into inactive styrene glycol, respectively. (Author abstract) (5 Refs)

299 AU - Norden AN
AD - Huntingdon Res. Center, Huntingdon, Cambridgeshire, England
TI - IMPACT ON DRUGS, FOOD, AND ENVIRONMENT.
SI - CARC/79/07096
SO - Proceedings of the 1st International Congress on Toxicology: Toxicology as a Predictive Science, held in Toronto, Canada, 30 March- 2 April 1977. Plaa GL, Duncan WA, ed. New York, Academic Press, Inc., 670 pp., 1978.
LA - ENG
AB - Modifications based on toxicological research could help diminish hazards such as those associated with smoking, including carcinogenicity. Cancer associated with inhalation of combustion products containing known carcinogens has decreased in the United Kingdom since 1955, and the hazards of exposure to mesothelioma-inducing asbestos particles could be reduced by reducing cigarette smoking. The predictive use of animal experimentation must be linked with postmarketing or postexposure monitoring and surveillance. Among the human environmental carcinogens which have been 'predicted' from animal experimentation are mustard gas, vinyl chloride, stilbestrol, and aflatoxin. Foods constitute the most complex group of substances from the standpoint of predictive toxicology. It is suggested that although toxicity testing might delay and added to the expense of the clearance of new medicines, it does not ultimately deprive mankind of valuable therapeutic agents. (85 Refs)

300 AU - Nelson N
AD - Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY
TI - ENVIRONMENTAL CANCER: INTERPLAY BETWEEN LABORATORY AND FIELD STUDIES.
SI - CARC/79/07093
SO - Proceedings of the 1st International Congress on Toxicology: Toxicology as a Predictive Science, held in Toronto, Canada, 30 March- 2 April 1977. Plaa GL, Duncan WA, ed. New York, Academic Press, Inc., 670 pp., 1978.
LA - ENG
AB - The respective roles of epidemiologic and laboratory studies in identifying specific factors leading to a particular cancer are

reviewed. The alkaline chromates have been identified as the agents of probable greatest importance in cancer induction by chromium. Extensive epidemiologic studies on the consequences of childhood scalp irradiation of children for control of ring worm were augmented by laboratory studies that identified the dose to various biological targets from the procedure. These studies led to the identification of eight thyroid adenomas in 1,500 exposed children at the very low dose of 6 rads to the thyroid. Cigarette smoking has been linked to lung cancer in many studies, but the specific carcinogenic factors have not yet been identified precisely. Cigarette smoke contains promoting and cocarcinogenic agents that substantially enhance the activity of the carcinogenic polynuclear hydrocarbons, and the combination of all these factors may produce the carcinogenic effects of cigarette smoke. Vinyl chloride and bis(chloromethyl)ether were identified as carcinogens in the laboratory in the absence of epidemiologic evidence. Subsequently, definitive epidemiologic studies confirmed that occupational cancers had resulted from exposure to these chemicals. A clear association was established between lung cancer and occupational exposure to the chloroethers. Dimethyl carbamoyl chloride has also been identified as carcinogenic in related studies. (22 Refs)

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