R&S 102653

P3104521

THIS IS AN OFF-LINE BIBLIOGRAPHIC CITATION LIST GENERATED BY

MEDLARS II

N.L.M.'S NATIONAL INTERACTIVE RETRIEVAL SERVICE

VINYL CHLORIDE, POLYVINYL CHLORIDE / CANCER-RELATED

NUMBER OF CITATIONS PRINTED = 74 JANUARY 14, 1988

THIS SEARCH WAS PERFORMED ON THE TOXLIT65 FILE.

SORT WAS NOT REQUESTED

REQUESTED BY
E. GRESCH

PLEASE SEND THIS LISTING TO

DIANE WROBLEWSKI
1803 BUILDING
MIDLAND, MICHIGAN 48640

1 AU - KRAJEWSKI J ; DOBECKI M ; GROMIEC J
AD - Dep. Chemical Air Pollutants Inst. Occupational Med., Lodz, Poland.
TI - Retention of vinyl chloride in the human lung.
SI - HEEP/81/09512
SO - BR J IND MED; 37 (4). 1980 (RECD. 1981). 373-374.
AB - HEEP COPYRIGHT: BIOL ABS. Experiments with volunteers showed that 42% of an inhaled dose of vinyl chloride (a carcinogen) was retained in the lungs. This value was independent of concentration of vinyl chloride in the air. Elimination of vinyl chloride through the lungs was negligible since its concentration in expired air decreased immediately after cessation of exposure.

2 AU - CORDASCO EM ; DEMETER SL ; KERKAY J ; VAN ORDSTRAND HS ; LUCAS EV
AU - CHEN T ; GOLISH JA
AD - 9500 Euclid Ave., Cleveland 44106.
TI - Pulmonary manifestations of vinyl chloride and polyvinyl chloride (interstitial lung disease): Newer aspects.
SI - HEEP/81/07600
SO - CHEST; 78 (6). 1980 (RECD. 1981). 828-834.
AB - HEEP COPYRIGHT: BIOL ABS. Newer varieties of occupational lung diseases primarily due to increased industrial technology were reported. Preeminent among newer agents were vinyl chloride (VC) and polyvinyl chloride. Few cases were reported, only in Europe, with descriptive histopathologic changes. No pathologic studies of VC exposure were described in USA literature. Biopsy abnormalities in patients disclosed desquamation of alveolar macrophages into alveolar lumina and minor interstitial and alveolar inflammatory changes. Pulmonary function abnormalities included restrictive insufficiency. Preventive therapy consisted of avoidance of further exposures, frequent industrial hygiene monitoring and total avoidance of tobacco smoke and associated atmospheric pollutants. No patient had exhibited evidence of pulmonary neoplasm. All 3 patients survived their occupational injuries and 2 were still disabled to varying degrees. Urine and blood levels of phthalic acid derivatives were elevated in 2 patients, exact significance was not fully known. It probably represented a toxicologic response.

3 AU - SMITH AH ; WAXWEILER RJ ; TYROLER HA
AD - Dep. Community Health, Wellington Clin. Sch. Med., Wellington Hosp., Wellington 2, N.Z.
TI - Epidemiologic investigation of occupational carcinogenesis using a serially additive expected dose model.
SI - HEEP/81/07562
SO - AM J EPIDEMIOL; 112 (6). 1980 (RECD. 1981). 787-797.
AB - HEEP COPYRIGHT: BIOL ABS. 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. Considering these problems, a method using the cumulative dose concept was developed; this

involves calculating the expected yearly exposure for each case from work histories of all noncases close to the case, in year of birth and year of hire. Data required for use of the method include information concerning exposure to the chemicals being studied for each job in each calendar year of the study. Use of the method is illustrated with a study of liver angiosarcoma 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 such as exposure level relationships, latency information and the possibility that 2 chemicals might be acting independently or jointly. The serially additive expected dose model may prove particularly useful in the analysis of data collected by occupational health surveillance systems, and in retrospective studies.

4 AU - BAXTER PJ ; ANTHONY PP ; MACSWEEN R NM ; SCHEUER PJ
AD - Employment Med. Adv. Serv., London NW1 5DT, Engl., UK.
TI - Angiosarcoma of the liver: Annual occurrence and etiology in Great Britain, UK.
SI - HEEP/81/01598
SO - BR J IND MED; 37 (3). 1980. 213-221.
AB - HEEP COPYRIGHT: BIOL ABS. The annual occurrence of angiosarcoma of the liver (ASL) in Britain from 1963-1977 was studied, including clinical and occupational details for those cases agreed as ASL by a panel of histopathologists. Cases (28 men, 6 women and 1 infant girl) were agreed as ASL. The increase in the incidence of ASL observed in recent years 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 metatases were found in only 8 (23%) cases, and hemoperitoneum was more common in those cases due to Thorotrast. There is 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 1 case was indicative of As intoxication, but medications in the other patients were not of etiological importance.

5 AU - SUZUKI Y
AD - Environ. Sci. Lab., Dep. Community Med., Mt. Sinai Sch. Med., City Univ. N.Y., One Gustave Levy Pl., New York, N.Y. 10029, USA.
TI - Nonneoplastic effects of vinyl chloride in mouse lung.
SI - HEEP/80/09794
SO - ENVIRON RES; 21 (1). 1980. 235-253.
AB - HEEP COPYRIGHT: BIOL ABS. In a previous study, a high incidence of pulmonary tumors (alveologenic neoplasia) in mouse lung exposed to vinyl chloride at heavy dose (2500 and 6000 ppm) for long durations (5 and 6 mo.) was reported (Y. Suzuki). In the present study, nonneoplastic effects in mouse lung were investigated by light microscopy and EM. 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 or 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.

6 AU - MURATOV MM ; TAKHIROV MT
TI - MAXIMUM PERMISSIBLE CONCENTRATION OF VINYL CHLORIDE IN AIR
SI - HEEP/81/09115
SO - GIG SANIT; 0 (11). 1979 (RECD. 1980). 74-76.
LA - RUS
AB - HEEP COPYRIGHT: BIOL ABS. NOTE HUMAN RAT CARCINOGEN RNA IMMUNITY MUTAGENICITY TEMPERATURE LIVER KIDNEY BRAIN HEART OCCUPATIONAL HEALTH

7 AU - PIALAT J ; PASQUIER B ; PHAN M ; KOPP N
AD - Lab. Anat. Pathol., Cent. Hosp. Univ. Lyon, Fac. Alexis Carrel, rue Guillaume-Paradin, 69372 Lyon Cedex 2, Fr.
TI - Hepatic lesions caused by vinyl chloride monomer in humans: 8 clinicopathological cases.
SI - HEEP/80/10961
SO - ARCH ANAT CYTOL PATHOL; 27 (6). 1979 (RECD. 1980). 361-375.
AB - HEEP COPYRIGHT: BIOL ABS. Six hepatic angiosarcomas, 1 hepatoma and 1 hepatic fibrosis with portal hypertension in patients chronically exposed to vinyl chloride monomer (VCM) are reported. The industrial methods of synthesis and current knowedge on the carcinogenic role of VCM are reviewed. Histogenetic and pathogenetic concepts of fibrosis and angiosarcomas of liver are discussed.

8 AU - DAVIS DL ; MAGEE BH
TI - CANCER AND INDUSTRIAL CHEMICAL PRODUCTION
SI - HEEP/80/10250
SO - SCIENCE (WASH D C); 206 (4425). 1979 (RECD. 1980). 1356, 1358.
LA - ENG
AB - HEEP COPYRIGHT: BIOL ABS. NOTE HUMAN BENZENE PER CHLOR ETHYLENE VINYL CHLORIDE ACRYLONITRILE ASBESTOS CHROMITE CHLOROFORM CARBON TETRA CHLORIDE TRI CHLOROETHYLENE CARCINOGEN LUNG CANCER SMOKING

9 AU - FERON VJ ; SPIT BJ ; IMMEL HR ; KROES R
AD - Dep. Toxicol., Cent. Inst. Nutr., P.O. Box 360, 3700 AJ Zeist, Neth.
TI - 1-year time-sequence inhalation toxicity study of vinyl chloride in rats: 3. Morphological changes in the liver.
SI - HEEP/80/06359
SO - TOXICOLOGY; 13 (2). 1979. 143-154.
AB - HEEP COPYRIGHT: BIOL ABS. Wistar rats were exposed to atmospheres containing 0 (control) or 5000 ppm vinyl chloride monomer (VCM), 7 h/day, 5 days/week, for 52 wk. After 4, 13, 26 and 52 weeks each time 10 rats/sex per group were killed and subjected to extensive examinations. The morphological changes found in the liver were described. The major parenchymal changes comprised swelling and malformation of mitochondria, an increased amount of smooth endoplasmic reticulum, necrosis, nuclear and cellular polymorphism of hepatocytes, foci of cellular alteration, neoplastic nodules and hepatocellular carcinomas. A reduced glucose-6-phosphatase activity in hepatocytes and a strong sinusoidal activity of alkaline phosphatase were found within foci of cellular alteration. The non-parenchymal alterations included focal dilatation of sinusoids, focal proliferation of atypical sinusoidal cells and multicentric angiosarcomas. The effects of VCM on the hepatic parenchyma seemed to precede those on the hepatic stroma.

10 AU - FERON VJ ; KROES R
AD - Dep. Toxicol., Cent. Inst. Nutr., P.O. Box 360, 3700 AJ Zeist, Neth.
TI - 1-year time-sequence inhalation toxicity study of vinyl chloride in rats: 2. Morphological changes in the respiratory tract, ceruminous glands, brain, kidneys, heart and spleen.
SI - HEEP/80/06358
SO - TOXICOLOGY; 13 (2). 1979. 131-142.
AB - HEEP COPYRIGHT: BIOL ABS. Wistar rats were exposed to atmospheres containing 0 (control) or 5000 ppm vinyl chloride monomer (VCM), 7 h/day, 5 days/wk, for 52 wk. After 4, 13, 26 and 52 wk each time 10 rats/sex per group were killed and subjected to extensive examinations. The morphological changes observed in the respiratory tract, ceruminous glands, brain, kidneys, heart and spleen were described. The VCM-effects included increased degree of tubular nephrosis, mild focal degeneration of the myocard and increased hematopoietic activity in the spleen. Primary tumors were found in the brain (ependymoma), lungs (papillary adenoma and mesenchymal type of tumor), ceruminous glands (mainly keratinized squamous cell carcinomas), and nasal cavity (carcinomas of the olfactory epithelium, carcino-sarcoma, esthesioneuroepithelioma).

11 AU - GEHRING PJ ; WATANABE PG ; PARK CN
AD - Toxicol. Res. Lab., Dow Chem. USA, Midland, Mich. 48640, USA.
TI - Risk of angiosarcoma in workers exposed to vinyl chloride as predicted from studies in rats.
SI - HEEP/80/01556
SO - TOXICOL APPL PHARMACOL; 49 (1). 1979. 15-22.
AB - HEEP COPYRIGHT: BIOL ABS. 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 whereas 5 have occurred. Linear models and that based on the equation, Risk = 1 - e-betax, where x = dose, do not appear as reliable. For an 8 h day, 5 days/wk, 35 yr time-weighted/average exposure of 1 ppm, the predicted incidence of hepatic angiosarcoma using the probit model is 1.5

12 AU - HALEY TJ
TI - CHLOROPRENE 2 CHLORO-1 3 BUTADIENE WHAT IS THE EVIDENCE FOR ITS CARCINOGENICITY
SI - HEEP/79/13416
SO - WINEK, CHARLES L. AND SYDNEY P. SHANOR (ED.). TOXICOLOGY ANNUAL, VOL. 3. XII+340P. ILLUS. MARCEL DEKKER, INC.: NEW YORK, N.Y., USA; BASEL, SWITZERLAND. ISBN 0-8247-6773-X.; 1979 153-170
AB - HEEP COPYRIGHT: BIOL ABS. HUMAN RAT MOUSE NERVOUS SYSTEM VINYL CHLORIDE CARCINOGEN OCCUPATIONAL EXPOSURE MIXED FUNCTION OXIDASE NERVOUS SYSTEM EFFECTS LUNG CANCER SKIN CANCER DENTAL EFFECTS

13 AU - ZUCCATO E ; MARCUCCI F ; FANELLI R ; MUSSINI E
AD - Ist. Ric. Farmacol. Mario Negri, Via Eritrea 62, 20157 Milan, Italy.
TI - Head-space gas-chromatographic analysis of vinyl chloride monomer in rat blood and tissues.
SI - HEEP/79/12436
SO - XENOBIOTICA; 9 (1). 1979. 27-32.
AB - HEEP COPYRIGHT: BIOL ABS. A method for measuring (the carcinogen) vinyl chloride monomer (VCM) concentration in rat blood and tissues is described, using a head-space GLC technique with flame ionization detector. The method is sensitive to 5 ng/ml VCM in blood and 30 ng/g in tissues. VCM disposition was determined in rat blood, liver, kidney, brain and lung at different intervals after administration of 1-10 mg VCM/kg i.v. and 10 mg/kg orally. VCM distributed rapidly in the organism after i.v. administration; it was eliminated rapidly and was no longer detectable at 15 min for the highest dose and at 4 min for the lowest. VCM was absorbed rapidly when given orally and tissue

concentrations were measurable for longer than after i.v. treatment. For both routes, VCM concentration in liver and lung decrease faster than in other organs, suggesting that these organs play a role in VCM elimination.

14 AU - BUFFLER PA ; WOOD S ; EIFLER C ; SUAREZ L ; KILIAN DJ
AD - Univ. Tex. Sch. Public Health, P.O. Box 20186, Houston, Tex. 77025, USA.
TI - Mortality experience of workers in a vinyl chloride monomer product plant.
SI - HEEP/79/10829
SO - J OCCUP MED; 21 (3). 1979. 195-203.
AB - HEEP COPYRIGHT: BIOL ABS. The evidence associating exposure to vinyl chloride with the risk of tumors of various sites, including lung cancer, is inconsistent. In 1976 a mortality follow-up study of 464 white males employed in a vinyl chloride monomer (VCM) production plant since 1948 was conducted. Vital status was ascertained for 100% of the cohort. Of the 28 deaths observed, 8 (28.5%) were due to malignant neoplasms. No angiosarcomas or other liver tumors were observed. A statistically significant excess was noted for malignant neoplasms of the respiratory system (P = .03). The effect of smoking, duration of exposure to VCM, 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. Levels of exposure to VCM prior to 1971 were estimated from monitoring data available for the period 1971-1975 by extrapolating the relative levels for job classifications backwards in time. Smoking histories were not available for 27.6% of the cohort. When it was assumed that all "unknowns" smoked, a significant excess of respiratory cancer was still observed (P = .05). When the minimum latency period of 5 yr restricted analysis to the mortality experience after 5 yr from date of initial exposure to VCM for the 314 employees satisfying this criterion, the excess of respiratory cancer was moderate but not significant (P = .06). Both a longer duration and a higher level of exposure during the first 5 yr following the date of initial exposure were associated with a statistically significant excess of respiratory cancer (P = .02 and .03, respectively). When duration and level of exposure were combined in an overall exposure index, the results were not significant (P = .07). The discrepancy in the results from the dose-response analyses may be due to the potential error in the estimated levels and the small number of events observed, but the results suggest that a relationship exists between exposure to VCM and respiratory cancer.

15 AU - CHEN K TK ; BOLLES JC ; GILBERT EF
AD - Dep. Pathol., Fresno Community Hosp., P.O. box 1232, Fresno, Calif. 93715, USA.
TI - Angiosarcoma of the spleen: A report of two cases and review of the literature.
SI - HEEP/79/09598
SO - ARCH PATHOL LAB MED; 103 (3). 1979. 122-124.
AB - HEEP COPYRIGHT: BIOL ABS. Ultrastructural study of 1 of 2 cases of splenic angiosarcoma established the blood vessel origin of this tumor. Previously reported cases (53) were reviewed. None of the 55 patients had a history of exposure to thorium dioxide, vinyl chloride or As, 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. Tumors associated with thorium dioxide, vinyl chloride, or As commonly involve the liver with sparing of the spleen.

16 AU - Bartsch H ; Sabadie N ; Malaveille C ; Camus AM
AU - Richter-Reichhelm HB
AD - Unit Chem. Carcinog., Int. Agency Res. Cancer, Lyon
TI - Carcinogen metabolism with human and experimental animal tissues: inter-individual and species differences
SI - CA/093/001946V
SO - Adv. Med. Oncol., Res. Educ., Proc. Int. Cancer Congr., 12th; VOL 3,, 1979,179-87
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Liver fractions obtained from surgery tissue samples of different human subjects were shown to convert vinyl chloride or related haloolefins and several N-nitroso derivs. into alkylating and mutagenic intermediates. (75-01-4 Vinyl chloride) Although large individual variations were obsd., the av. activity was lower or close to mouse or rat liver fractions. However, with N-nitroso-N'-methylpiperazine, human liver samples were up to 40 times more active than rat liver. When hepatic benzo[a]pyrene hydroxylase (BP hydroxylase) activity in samples from different human subjects was plotted against the liver microsome-mediated mutagenicity, a pos. correlation was obtained between the rates of oxidative BP metab. and mutagenicity in the presence of N-nitrosomorpholine or vinyl chloride as substrate. (16339-07-4 N-Nitroso-N'-methylpiperazine)(9037-52-9 benzo[a]pyrene hydroxylase)(59-89-2 N-Nitrosomorpholine) Therefore, BP hydroxylase activity in normal and tumorous lung tissue from 76 patients with lung tumors was measured. A 60-fold interindividual variation was noted with the rates of BP hydroxylation in tumorous lung tissue lower than in normal tissue of the same patient. When BP hydroxylase activity in the tumorous tissue was plotted vs. the no. of cigarets smoked per day prior to surgery, a neg. correlation was apparent. Thus, differences in carcinogenic metab. may condition in part the

response of human individuals when exposed to the same level of environmental carcinogens.

17 AU - Brundrett RB ; Colvin M ; White EH ; McKee J ; Hartman PE
AU - Brown OL
AD - Dep. Chem., Johns Hopkins Univ., Baltimore
TI - Comparison of mutagenicity, antitumor activity, and chemical properties of selected nitrosoureas and nitrosoamides
SI - CA/091/032798M
SO - Cancer Res.; VOL 39, ISS 4, 1979,1328-33
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Nitroureas and nitrosoamides were compared with respect to mutagenicity for Salmonella typhimurium, in vitro cytotoxicity, in vitro toxicity and antitumor activity against murine leukemia, and chem. properties. Despite chem. similarities between the nitroureas and nitrosoamides, they showed important differences in biol. activity. Some of the nitrosoureas were very active antitumor agents, and less mutagenic than the corresponding nitrosoamides, which lacked antitumor activity.

18 AU - Feron VJ ; Kroes R
AD - Cent. Inst. Nutr. Food Res., TNO, Zeist
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 - CA/092/016860R
SO - Toxicology; VOL 13, ISS 2, 1979,131-41
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Rats were exposed to atms. contg. 0 (control) or 5000 ppm vinyl chloride monomer (VCM), 7 h/day, 5 days/wk, for a period of 52 wk. (75-01-4 Vinyl chloride) After 4, 13, 26 and 52 wk 10 rats/sex/group were killed and subjected to extensive exams. VCM-induced effects included an increase in the degree of tubular nephrosis, mild focal degeneration of the myocardium, and increased hematopoietic activity in the spleen. In addn., primary tumors were found in the brain (ependymoma), lungs (papillary adenoma and mesenchymal-type of tumor), ceruminous glands (mainly keratinized squamous cell carcinomas), and nasal cavity (carcinomas of the olfactory epithelium, carcinosarcoma, and esthesioneuroepithelioma).

19 AU - Feron VJ ; Spit BJ ; Immel HR ; Kroes R
AD - Cent. Inst. Nutr. Food Res., TNO, Zeist
TI - One-year time-sequence inhalation toxicity study of vinyl chloride in rats. III. Morphological changes in the liver
SI - CA/092/016616R
SO - Toxicology; VOL 13, ISS 2, 1979,143-54
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Rats were exposed to atmospheres contg. 0 (control) or 5000 ppm vinyl chloride monomer (VCM), 7 h/day, 5 days/wk, for a period of 52 wk. (75-01-4 Vinyl chloride) After 4, 13, 26 and 52 wk 10 rats/sex/group were

killed and subjected to extensive examns. The major parenchymal changes comprised swelling and malformation of mitochondria, an increased amt. of smooth endoplasmic reticulum, necrosis, nuclear and cellular polymorphism of hepatocytes, foci of cellular alteration, neoplastic nodules and hepatocellular carcinomas. A reduced glucose 6-phosphatase activity in hepatocytes and a strong sinusoidal activity of alk. phosphatase were found within foci of cellular alteration. (9001-78-9 Alkaline phosphatase)(9001-78-9 alk. phosphatase) The nonparenchymal alterations included focal dilation of sinusoids focal proliferation of atypical sinusoidal cells and multicentric angiosarcomas. The effect of VCM on the hepatic parenchyma seemed to precede those on the hepatic stroma.

20 AU - DAHL GA ; MILLER JA ; MILLER EC
AD - McArdle Lab. Cancer Res., Univ. Wis. Cent. Health Sci., Madison, Wis. 53706, USA.
TI - Vinyl carbamate as a promutagen and a more carcinogenic analog of ethyl carbamate.
SI - HEEP/79/05120
SO - CANCER RES; 38 ((11 PART 1)). 1978 3793-3804
AB - HEEP COPYRIGHT: BIOL ABS. Vinyl carbamate was much more active (10 to 50 times) than ethyl carbamate for the initiation of skin tumors and for the induction of lung adenomas in mice. Vinyl carbamate was also mutagenic to Salmonella typhimurium TA 1535 and TA 100 in the presence of NADPH-fortified rat or mouse liver mitochondrial supernatant fractions. This mutagenic activity was inhibited strongly by cytochrome P-450 inhibitors. No mutagenic activity was observed for vinyl carbamate in the absence of added liver preparations or for ethyl carbamate in the presence or absence of liver fractions. Extensive tests with sensitive methods failed to detect vinyl carbamate as a metabolite of ethyl carbamate in the mouse in vivo. However, on administration of (ethyl-1- 14C;1,2-3H)ethyl carbamate to adult mice the 3H/14C ratios of the hepatic DNA-, rRNA-, and protein-adducts were similar to each other and much lower than the ratio of the administered ethyl carbamate. These data are consistent with the presence of desaturated and/or oxidized ethyl groups in the macromolecular adducts. The qualitatively similar, but much stronger, carcinogenic activity of vinyl carbamate as compared to that of ethyl carbamate suggests that the metabolic pathways of these two carbamates may converge in the formation of similar or identical electrophilic reactants that bind covalently to macromolecules in vivo and initiate carcinogenesis.

21 AU - DELORME F ; THERIAULT G
AD - Dep. Pathol., Cent. Hosp. Reg. Maurice, Shawinigan, Que., Can.
TI - Ten cases of angiosarcoma of the liver in Shawinigan, Quebec.
SI - HEEP/79/03983
SO - J OCCUP MED; 20 (5). 1978 338-340
AB - HEEP COPYRIGHT: BIOL ABS. Ten cases of angiosarcoma of the liver have been diagnosed in Shawinigan, Quebec (Canada) since 1955. All have occurred in men who worked in a vinyl chloride

polymerizing plant. Cigarettes and alcohol did not seem to be associated with this tumor. The amount of vinyl chloride to which these people were exposed, according to information obtained through questionnaires, appears elevated. Angiosarcoma of the liver was accompanied by a fibrosis of the liver which may precede its appearance. In describing the Canadian cases of angiosarcoma, this study attempted to shed more light upon the causal relationship between vinyl chloride monomer and angiosarcoma of the liver and to provide some clues to understanding the pathogenesis of this disease.

22 AU - DELORME F
AD - Cent. Hosp. Reg. Mauricie, CP 1130, Shawinigan-Sud, Que., Can.
TI - Association of angiosarcoma of the liver with hepatoma in a vinyl chloride worker.
SI - HEEP/79/03980
SO - ANN ANAT PATHOL; 23 (2). 1978 105-113
AB - HEEP COPYRIGHT: BIOL ABS. This report deals with a 51 yr-old man who, for 23 yr and 4 mo. of his working life, was exposed to vinyl chloride vapors. Autopsy revealed a hepatoma associated with an angiosarcoma of the liver. The case is the 1st ever to be reported in the medical litterature. This case raises doubts about the theory which suggests that the carcinogenic effect of vinyl chloride in man elicit a tumor of vascular nature.

23 AU - VAN DUUREN BL ; LOEWENGART G ; SEIDMAN I ; SMITH AC ; MELCHIONNE S
AD - Lab. Org. Chem. Carcinog., Inst. Environ. Med., N.Y. Univ. Med. Cent., New York, N.Y. 10016, USA.
TI - Mouse skin carcinogenicity tests of the flame retardants tris(2,3-dibromopropyl)phosphate, tetrakis(hydroxymethyl)phosphonium chloride, and polyvinyl bromide.
SI - HEEP/79/03540
SO - CANCER RES; 38 (10). 1978 3236-3240
AB - HEEP COPYRIGHT: BIOL ABS. The flame retardants tris(2,3-dibromopropyl)phosphate, tetrakis(hydroxymethyl)phosphonium chloride and polyvinyl bromide were tested for carcinogenic activity by skin application 3 times weekly in random-bred female ICR/Ha Swiss mice for 420-496 days. Tris(2,3-dibromopropyl)phosphate at 2 dose levels (30 and 10 mg/application) induced benign and malignant tumors of the skin, forestomach and oral cavity (tongue and gingiva) in a statistically significant number of mice (30/group). A statistically significant incidence of papillary tumors of the lung was observed at both dosages. One carcinoma of the liver was observed at both doses, and the higher dose also resulted in 1 mouse with a tubular adenoma of the kidney. Tetrakis(hydroxymethyl)phosphonium chloride (2 mg/application, 60 mice) and polyvinyl bromide (0.1 ml latex suspension/application, 30 mice) were inactive. Polyvinyl bromide was also injected s.c. into another group of female ICR/Ha Swiss mice once weekly for 48 wk, and the mice were observed for a total of 60 wk. Liposarcomas were induced in 19 of 30 mice, which was ascribed to physical

carcinogenesis. Appropriate solvent and no-treatment control groups were included.

24 AU - WATANABE PG ; ZEMPEL JA ; PEGG DG ; GEHRING PJ
AD - Toxicol. Res. Lab., Health Environ. Res., 1803 Build., Dow Chem. Co., Midland, Mich. 48640, USA.
TI - Hepatic macromolecular binding following exposure to vinyl chloride.
SI - HEEP/79/02717
SO - TOXICOL APPL PHARMACOL; 44 (3). 1978 571-580
AB - HEEP COPYRIGHT: BIOL ABS. Covalent binding of radioactivity to hepatic macromolecules in rats exposed to 14C-labeled vinyl chloride (VC) was studied to determine if VC-induced carcinogenesis may be related to electrophilic alkylation of macromolecules in vivo. Male Sprague-Dawley rats were exposed to 1, 10, 25, 50, 100, 250, 500 or 5000 ppm of (14C)VC for 6 h. Following exposure, radioactivity covalently bound to hepatic macromolecules and purified nucleic acids (RNA, DNA) was determined. The total amount of (14C)VC metabolized and hepatic glutathione (GSH) content were also determined. The total amount of radioactivity bound to macromolecules in the liver did not increase proportionately to the increase in the exposure concentration of VC. A disproportionate decrease in macromolecular binding was observed as the concentration of VC increased. Covalent binding to hepatic macromolecules was related to the amount of VC metabolized. At exposures greater than 50 ppm, the amount of 14C bound to macromolecules in the liver correlates with induction of hepatic angiosarcoma. There was no detectable binding of radioactivity to DNA or RNA in the liver. Hepatic glutathione content was significantly depressed only at exposure concentrations greater than 100 ppm.

25 AU - POPPER H ; THOMAS LB ; TELLES NC ; FALK H ; SELIKOFF IJ
AD - Lab. Pathol., Natl. Cancer Inst., Room 2A27, Build. 10, Bethesda, Md. 20014, USA.
TI - Development of hepatic angiosarcoma in man induced by vinyl chloride, Thorotrast, and arsenic: Comparison with cases of unknown etiology.
SI - HEEP/79/02712
SO - AM J PATHOL; 92 (2). 1978 349-376
AB - HEEP COPYRIGHT: BIOL ABS. Examples of human angiosarcoma following exposure to vinyl chloride, Thorotrast or As (medicinal and industrial) and cases, including children, of unknown etiology were studied to establish diagnostic criteria and to study their evolution. The uniform evolution suggests an environmental factor also in the cases of unknown etiology, which may be established by epidemiologic studies. A precursor stage is characterized by areas of combined hyperplasia of hepatocytes and a variety of sinusoidal and perisinusoidal cells associated with excess of reticulin and sinusoidal dilatation. The diagnostically useful picture in Ag impregnations indicates reticulum formation by the perisinusoidal cells, presumably the lipocytes. The hepatocytic proliferation suggests a hepatocarcinogenic but

usually not fully expressed potential. The mixed hyperplasia of the various sinusoidal cells proceeds to an overgrowth of angiosarcoma cells, presumably derived from endothelial cells. In early stages they are usually in contact with hepatocytes (intralobular growth). A trabecular arrangement results from loosening of the lobular plate arrangement by dilatation of sinusoids, leading to primary peliosis. With disappearance of the hepatocytes, various growth patterns develop, terminating in nodular, solid angiosarcoma composed of spindle-shaped or polyhedral cells which undergo necrosis or hemorrhage (secondary peliosis). The interaction between hepatocytes and sinusoidal cells requires elucidation.

26 AU - SUZUKI Y
AD - Environ. Sci. Lab., Mt. Sinai Sch. Med., Fifth Ave. and 100th St., New York, N.Y. 10029, USA.
TI - Pulmonary tumors induced in mice by vinyl chloride monomer.
SI - HEEP/79/02364
SO - ENVIRON RES; 16 (1-3). 1978 285-301
AB - HEEP COPYRIGHT: BIOL ABS. Neoplastic effects of vinyl chloride were studied in lungs of 27 mice exposed to vinyl chloride monomer at 2500 and 6000 ppm for 5 and 6 mo. Pulmonary tumors were observed in 26 of 27 experimental animals. By light microscopy, the tumors were multiple and arranged in either tubulo-papillary or adenomatous formations. Although occasional mitotic divisions and invaginations into the bronchiolar lumen were observed, no metastases were found. By EM, short microvilli, tight junctions between 2 adjacent cells, appearance of osmiophilic lamellar bodies, large mitochondria of irregular shape, well-developed Golgi complexes, continuous or discontinuous basement membranes, occasional appearance of sequestration and of crystalloids, and lack of both cilia and mucous secretory granules were observed as characteristic features of the neoplastic cells. Some of the cells were poorly differentiated and were equipped with poorly developed organoids, without formation of osmiophilic lamellar bodies. The pulmonary tumors corresponded to alveologenic tumors or alveologenic cancer. The neoplastic cells were probably transformed from type II alveolar epithelium via its hyperplastic form. Mouse lung is an extremely sensitive indicator of the oncogenicity of vinyl chloride.

27 AU - TAMBURRO CH
AD - Dig. Dis. Nutr. Div., 511 S. Floyd St., PO Box 35260, Louisville, Ky. 40232, USA.
TI - The hepatic role in carcinogenesis and its early detection: The vinyl chloride model.
SI - HEEP/79/00115
SO - YALE J BIOL MED; 51 (1). 1978 67-80
AB - HEEP COPYRIGHT: BIOL ABS. The liver's role in vinyl chloride toxicity and carcinogenicity is providing a better understanding of the chemical carcinogenesis mechanism. A variety of malignant and benign hepatic tumors was demonstrated with prolonged

exposure to vinyl chloride. The multisystem involvement of this carcinogen and toxin provided a model for the study of chemical carcinogenesis common to man and animal. Clinical studies showed the usefulness of biochemical, radioisotopic and radiological studies in the detection of toxic and carcinogenic lesions. Animal studies demonstrated the biochemical metabolism by the liver of vinyl chloride-produced intermediates which are mutagenic in bacterial systems and may be the ultimate carcinogens. Hepatic subcellular enzyme studies prove preliminary evidence of cellular adaptation and increased detoxification. Disruption of this oxidization and detoxification balance may be the key to malignant transformation of cells. A working hypothesis is presented which may explain the metabolism of vinyl chloride into mutagenic intermediates by liver cells and the development of malignant transformation by extrahepatic sinusoidal lining cells, lung cells and brain tissue.

28 AU - LEE CC ; BHANDARI JC ; WINSTON JM ; HOUSE WB ; DIXON RL ; WOODS JS
AD - Midwest Res. Inst., 425 Volker Blvd., Kansas City, Mo. 64110, USA.
TI - Carcinogenicity of vinyl chloride and vinylidene chloride.
SI - HEEP/78/10445
SO - J TOXICOL ENVIRON HEALTH; 4 (1). 1978 15-30
AB - HEEP COPYRIGHT: BIOL ABS. Exposure of mice to 50, 250 or 1000 ppm of vinyl chloride (VC) in the air for 6 h/day, 5 days/wk, caused a high incidence of bronchioloalveolar adenoma, mammary gland tumors and hemangiosarcoma. Mammary gland tumors occurred in females and included ductular adenocarcinoma and squamous and anaplastic cell carcinomas with metastases to the lungs. Hemangiosarcoma occurred in the liver and, to a lesser extent, in various other organs. The incidence and severity of these tumors increased with the concentration of VC and length of exposure. Malignant lymphoma involving various organs was observed in several mice. Rats were more resistant to the carcinogenic effects of VC. Exposure of rats to 250 or 1000 ppm of VC caused hemangiosarcoma in the liver. Many rats with hepatic hemangiosarcoma also developed hemangiosarcoma in the lung. Extrahepatic hemangiosarcoma also occasionally occurred in other organs. Exposure to 55 ppm of vinylidine chloride (VDC) caused hepatic hemangiosarcoma and probably bronchioloalveolar adenoma in mice. Hemangiosarcoma also occurred in the mesenteric lymph node or subcutaneous tissue in 2 rats exposed to 55 ppm of VDC.

29 AU - Milby TH
AD - SRI Int., Menlo Park
TI - Vinyl chloride - an information resource
SI - CA/092/081459F
SO - Report; ISS NIH-78/1599, DHEW/PUB/NIH-78/1599; Order No. HRP-0028012,, 1978,122 pp.
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS A discussion of the link between exposure to vinyl chloride (I) and the occurrence of toxic, nonmalignant illnesses involving skin, bones, liver, lungs, and blood is provided. (75-01-4 Vinyl chloride) The regulatory

R&S 102666

history of I is outlined. The potential for human contact with I is great. About 2.5 billion kg of I are produced each year in the United States. I is produced at 15 plants employing 900 workers. I is also polymd. at 39 plants, employing more than 5,500 workers. The Environmental Protection Agency has estd. that approx. 5 million people live near enough to I facilities to be within range of detectable airborne concns. of the gas. The prodn., uses, and dispersion of I are discussed, evidence of its toxic and carcinogenic effects are summarized, and strategies for its control are suggested. The appendices contain a list of I-related compds., an approach to evaluation and control of I exposure, and sources for addnl. information.

30 AU - Costa V ; Frongia N
AD - Univ. Cagliari, Cagliari
TI - Histological and ultrastructural study of the peritoneal changes induced by the endoabdominal inoculation of a single dose of poly(vinyl chloride) powder (PVC) in rats
SI - CA/091/152238A
SO - Rass. Med. Sarda; VOL 81, ISS 4, 1978,217-35
LA - ITA
AB - CBAC COPYRIGHT: CHEM ABS In rats i.p. administration of PVC resulted in granulomas of the peritoneum. (9002-86-2 Poly(vinyl chloride)) No neoplastic or preneoplastic alterations were obsd. Histopathol. changes of the lung, liver, and spleen, were also obsd.

31 AU - Anderson HA ; Snyder J ; Lewinson T ; Woo C ; Lilis R
AU - Selikoff IJ
AD - Mt. Sinai Sch. Med., City Univ. New York, New York, N. Y.
TI - Levels of CEA among vinyl chloride and poly(vinyl chloride)-exposed workers
SI - CA/090/043308G
SO - Cancer (Philadelphia); VOL 42, ISS 3, Suppl., 1978,1560-7
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS In 1974, vinyl chloride (VC) exposed workers had an increased risk of malignant disease (hemangiosarcoma of the liver). (75-01-4 Vinyl chloride) Thus 1147 workers exposed to VC monomer in 3 VC/poly(vinyl chloride) (PVC) . plants and 269 workers from a PVC extrusion plant manufg. PVC textile product, exposed to much lower concns. of VC were examd. (9002-86-2 Poly(vinyl chloride)) Included among the comprehensive clin. and lab. studies conducted was the CEA (carcinoembryonic antigen) titer. The investigation demonstrated that occupational exposures in VC/PVC plants can cause elevations in the CEA titers of otherwise healthy individuals. Prospective follow-up is necessary before conclusions can be drawn concerning the usefulness of the CEA titer as a predictive indicator of possible increased risk.

32 AU - Winell M ; Holmberg B ; Kronevi T
AD - Unit Occup. Toxicol., Natl. Board Occup. Saf. Health, Swed.
TI - A possible correlation between biochemical changes and pathological findings in VCM-exposed mice and hamsters
SI - CA/090/034611Y
SO - Int. Symp. Control Air Pollut. Work. Environ., [Proc.]; VOL Part 1,, 1978,152-66
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Mice and hamsters were exposed by inhalation to 50 and/or 500 ppm vinyl chloride monomer (VCM) during 6-18 mo. (75-01-4 Vinyl chloride) Blood samples were taken at regular intervals during the exposure for anal. of plasma enzymes indicative of liver damage or early malignancy. Some animals were sacrificed for histopathol. examns. after 6 mo and the rest were exam'd. when dead or moribund. Alk. phosphatase and total lactate dehydrogenase (LDH) activities were elevated in VCM exposed mice. There was also a shift towards cathodic isoenzymes of LDH. The transaminases were not significantly elevated. No changes in plasma enzymes were found in exposed hamsters. Pathol. examn. of VCM-exposed mice showed the presence of hemangiosarcomas in fat tissue, histol. benign alveologenic lung adenomas as well as a few benign and malignant tumors at various sites. Only 1 liver hemangiosarcoma was noted. No liver fibrosis was seen. All mice exposed to 50 ppm VCM for 76 mo developed tumors. Tumor incidence was high also in the hamsters. Enzyme changes occurred late in the study, subsequent to tumor appearance. The value of enzyme changes as a diagnostic criterion on tissue injury or early malignancy caused by VCM was discussed.

33 AU - INFANTE PF
TI - MUTAGENIC AND CARCINOGENIC RISKS ASSOCIATED WITH HALOGENATED OLEFINS
SI - HEEP/79/06563
SO - ENVIRON HEALTH PERSPECT; (21). 1977 (RECD 1978) 251-254
AB - HEEP COPYRIGHT: BIOL ABS. MOUSE RAT HUMAN SALMONELLA-TYPHIMURIUM DROSOPHILA VINYL CHLORIDE VINYLIDENE CHLORIDE TRI CHLORO ETHYLENE CARCINOGENS OCCUPATIONAL EXPOSURE CHROMOSOMAL ABERRATIONS LUNG SKIN CANCERS

34 AU - LEE C-C ; BHANDARI JC ; WINSTON JM ; HOUSE WB ; PETERS PJ
AU - DIXON RL ; WOODS JS
TI - INHALATION TOXICITY OF VINYL CHLORIDE AND VINYLIDENE CHLORIDE
SI - HEEP/79/06537
SO - ENVIRON HEALTH PERSPECT; (21). 1977 (RECD 1978) 25-32
AB - HEEP COPYRIGHT: BIOL ABS. MOUSE RAT MAMMARY GLAND LIVER LUNG KIDNEY DISEASES CARCINOMAS

35 AU - MALTONI C
TI - RECENT FINDINGS ON THE CARCINOGENICITY OF CHLORINATED OLEFINS
SI - HEEP/79/06534
SO - ENVIRON HEALTH PERSPECT; (21). 1977 (RECD 1978) 1-5
AB - HEEP COPYRIGHT: BIOL ABS. RAT MOUSE HAMSTER VINYL CHLORIDE VINYLIDENE CHLORIDE STYRENE ACRYLO NITRILE DI CHLORO ETHANE CHLORO FLUORO CARBONS TRI CHLORO ETHYLENE CARBON TETRA CHLORIDE VINYLIDENE FLUORIDE CARCINOGENS SKIN MAMMARY LEUKEMIA FORE STOMACH TUMORS LYMPHOMA

36 AU - WINSTON JM ; LEE CC ; BHANDARI JC ; DIXON RL ; WOODS JS
TI - A STUDY OF THE CARCINOGENICITY OF INHALED VINYL CHLORIDE AND VINYLIDENE CHLORIDE IN RATS AND MICE
SI - HEEP/78/07448
SO - BURFORD, R. G. INTERNATIONAL CONGRESS ON TOXICOLOGY. ABSTRACTS. TORONTO, ONTARIO, CANADA. 52P. INTERNATIONAL CONGRESS ON TOXICOLOGY: TORONTO, ONTARIO, CANADA.; 1977 32
AB - HEEP COPYRIGHT: BIOL ABS. ABSTRACT CARCINOGENS SKIN LUNG BONE LIVER MAMMARY TUMORS BRONCHIOLAR ADENOMA LIVER HEM ANGIO SARCOMA MALIGNANT LYMPHOMA

37 AU - ARYANPUR J
AD - Public Health Occup. Med. Serv., Natl. Iranian Oil Co., P.O. Box 1863, Tehran, Iran.
TI - Vinyl chloride: Its impact on occupational medicine practice in Iran.
SI - HEEP/78/06299
SO - J OCCUP MED; 19 (10). 1977 689-692
AB - HEEP COPYRIGHT: BIOL ABS. Awareness that VCM (vinyl chloride medicine) has been demonstrated to be a carcinogen producing a rare tumor, angiosarcoma, has led the company to tighten its medical monitoring and industrial hygiene controls. A temporary TLV (threshold limiting value) was established for VCM at 25 ppm consistent with the operating procedures of the company and local geographical conditions. The potential harm from industrial chemicals has stimulated the government and the company to support further control of inplant and outplant environmental hazards from industrial operations.

38 AU - CHIAZZE L JR ; NICHOLS WE ; WONG O
AD - Div. Biostatist. Epidemiol., Dep. Community Med. Int. Health, Georgetown Univ. Sch. Med., Washington, D.C. 20007, USA.
TI - Mortality among employees of PVC fabricators.
SI - HEEP/78/03515
SO - J OCCUP MED; 19 (9). 1977 623-628
AB - HEEP COPYRIGHT: BIOL ABS. A cross-sectional mortality study of 4341 deaths occurring among current and former employees of 17 PVC (polyvinyl chloride) fabricators during 1964-1973 is presented. The objectives were to identify any angiosarcoma deaths among the employees of these fabricators and to examine distribution of deaths by cause. No angiosarcoma deaths were found among the study group. Sex-race-cause-specific

Proportionate Mortality Ratios (PMR) were computed, using the corresponding USA mortality as the standard. Among white employees, there appeared to be an excess in total cancer mortality, particularly that of the digestive system. Observed deaths apparently exceeded those expected in cancers of the breast and urinary organs among white females. Deficit mortality was observed in cirrhosis of liver among male and female white employees.

39 AU - FOX AJ ; COLLIER PF
AD - Off. Pop. Censuses Surv., St. Catherines House, 10 Kingsway, London WC2B 6JP, Engl., UK.
TI - Mortality experience of workers exposed to vinyl chloride monomer in the manufacture of polyvinyl chloride in Great Britain.
SI - HEEP/78/01417
SO - BR J IND MED; 34 (1). 1977 1-10
AB - HEEP COPYRIGHT: BIOL ABS. Identification particulars were obtained for over 7000 men who were at some time between 1940-1974 exposed to vinyl chloride monomer in the manufacture of polyvinyl chloride. Approximately 99% of these men were traced and their mortality experience studied. The overall standardized mortality ratio, 75.4, shows a significant reduction compared with the national rates. Four cases of liver cancer were found; 2 were confirmed by a panel of liver pathologists as angiosarcoma and 2 as not angiosarcoma. There is no evidence to support the hypothesis that cancers other than those of the liver are associated with exposure to vinyl chlodrie monomer. The 2 cases of angiosarcoma were found in men who were exposed to high concentrations of the monomer although the 2nd man died only 8 yr after 1st exposure. The industry in Great Britain has expanded considerably since the 2nd World War with over 50% of men having entered within the last decade.

40 AU - NICHOLSON WJ
TI - CANCER FOLLOWING OCCUPATIONAL EXPOSURE TO ASBESTOS AND VINYL CHLORIDE
SI - HEEP/77/12051
SO - CANCER (PHILA); 39 (SUPPL 4). 1977 1792-1801
AB - HEEP COPYRIGHT: BIOL ABS. HUMAN CARCINOGENS LUNG CANCER

41 AU - Ikeda M
AD - Tohoku Univ. Sci. Med., Sendai, Japan
TI - Tumorigenicity of chlorinated ethylenes
SI - CA/087/162267R
SO - Igaku No Ayumi; VOL 102, ISS 6/7, 1977,453-9
LA - JPN
AB - CBAC COPYRIGHT: CHEM ABS A review with 17 refs. of the induction of liver angiosarcoma, hepatocellular carcinoma, nephroblastoma, pulmonary tumor, kidney adenocarcinoma, and mammary carcinoma by vinyl chloride, vinylidene chloride, trichloro- and tetrachloroethylene in rats and mice, including correlation of the effects to dose, age, and sex. (75-01-4 Vinyl chloride)(75-35-4 vinylidene chloride)(79-01-6

Trichloroethylene)(127-18-4 Tetrachloroethylene)

42 AU - Radike MJ ; Stemmer KL ; Brown PG ; Larson E ; Bingham E
AD - Inst. Environ. Health, Univ. Cincinnati, Cincinnati, Ohio
TI - Effect of ethanol and vinyl chloride on the induction of liver tumors: preliminary report
SI - CA/089/018137X
SO - Environ. Health Perspect.; VOL 21,, 1977,153-5
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS In rats exposed to 600 ppm vinyl chloride (I) and I plus 5% EtOH that were autopsied, the latent period for angiosarcoma of the liver to appear was 53 wk in rats exposed only to I and 38 wk in rats exposed to I and 5% EtOH. (75-01-4 Vinyl chloride)(64-17-5 Ethanol) Thus, there is a synergism between ingested EtOH and inhaled vinyl chloride in the induction of tumors.

dup Medline

43 AU - BARTSCH H ; MALAVEILLE C ; MONTESANO R
TI - THE PREDICTIVE VALUE OF TISSUE MEDIATED MUTAGENICITY ASSAYS TO ASSESS THE CARCINOGENIC RISK OF CHEMICALS
SI - HEEP/77/08776
SO - MONTESANO, R., H. BARTSCH AND L. TOMATIS (ED.). IARC (INTERNATIONAL AGENCY FOR RESEARCH ON CANCER) SCIENTIFIC PUBLICATIONS, NO. 12. SCREENING TESTS IN CHEMICAL CARCINOGENESIS. PROCEEDINGS OF A WORKSHOP BRUSSELS, BELGIUM, JUNE 9-12, 1975. XX+666P. ILLUS. INTERNATIONAL AGENCY FOR RESEARCH ON CANCER: LYON, FRANCE.; 1976 467-486
AB - HEEP COPYRIGHT: BIOL ABS. HUMAN MOUSE RAT SALMONELLA-TYPHIMURIUM NITROSAMINES VINYL CHLORIDE VINYLIDENE CHLORIDE 2 CHLORO BUTADIENE CARCINOGENS LUNG LIVER KIDNEY TISSUE

44 AU - GOKEL JM ; LIEBEZEIT E ; EDER M
AD - Pathol. Inst., Univ., Thalkirchner Str. 36, D-8000 Muenchen 2, W. Ger.
TI - Hemangiosarcoma and hepatocellular carcinoma of the liver following vinyl chloride exposure: A report of two cases.
SI - HEEP/77/07005
SO - VIRCHOWS ARCH A PATHOL ANAT HISTOL; 372 (3). 1976 (RECD 1977) 195-203
AB - HEEP COPYRIGHT: BIOL ABS. A report is given of the clinical and autopsy findings of 2 men who died from malignant liver neoplasms following occupational exposure to vinyl chloride. The 1st patient was a 44 yr old man with a hemangiosarcoma of the liver. The 2nd patient was a 67 yr old man with a hepatocellular carcinoma. Hepatocellular carcinoma due to vinyl chloride was not yet observed in man. Its occurrence was suggested from the results of animal experiments. The connection of hepatocellular carcinoma with exposure to vinyl chloride is discussed.

45 AU - PAGE M ; THERIAULT L ; DELORME F
AD - Hotel-Dieu Que., 11 Cote Palais, Que. G1R 2J6, Can.
TI - Elevated CEA levels in polyvinyl chloride workers.
SI - HEEP/77/06758
SO - BIOMED EXPRESS (PARIS); 25 (8). 1976 279
AB - HEEP COPYRIGHT: BIOL ABS. Plasma CEA (carcinoembryonic antigen) titer was measured in 200 polyvinyl chloride workers. A positive test was obtained in 48.3% of this high risk population as compared to 9.2% for a normal healthy population. CEA monitoring may be helpful in detecting early liver angiosarcoma.

46 AU - INFANTE PF ; WAGONER JK ; WAXWEILER RJ
TI - CARCINOGENIC MUTAGENIC AND TERATOGENIC RISKS ASSOCIATED WITH VINYL CHLORIDE
SI - HEEP/77/06571
SO - MUTAT RES; 41 (1). 1976 131-142
AB - HEEP COPYRIGHT: BIOL ABS. HUMAN ANIMAL LIVER ANGIO SARCOMA BRAIN CENTRAL NERVOUS SYSTEM RESPIRATORY LYMPHATIC HEMATOPOIETIC SYSTEM TUMORS OCCUPATIONAL EXPOSURE

47 AU - SHABAD LM ; GENIN VA
AD - Inst. Clin. Exp. Oncol., Acad. Med. Sci. USSR, Moscow, USSR.
TI - A new type of occupational malignant neoplasms induced by vinyl chloride: Review of literature.
SI - HEEP/77/05642
SO - GIG TR PROF ZABOL; (7). 1976 41-44
AB - HEEP COPYRIGHT: BIOL ABS. A review is given of malignant neoplasms in humans and laboratory animals associated with exposure to vinyl chloride or polyvinylchloride resins. Angiosarcoma and various functional impairments of the liver plus malignancies of the lymphatic and hematopoietic tissue, glioblastoma and tumors of the pancreas and skin were reported in workers or nearby residents exposed to atmospheric pollution from polyvinylchloride production. Laboratory animals developed adenoma, adenocarcinoma of the lungs and mammary glands, liver angiocarcinoma and other malignancies. Data are given on production of the carcinogen in western countries and Japan, and measures of prophylaxis, including establishment of maximum permissable concentrations, taken since the 1974 designation of vinyl chloride as a carcinogen. No cases of occupational cancer induced by vinyl chloride were registered in the USSR.

48 AU - FIECHTNER JJ ; REYES C N JR
AD - Marshfield Clin., 1000 N. Oak Ave., Marshfield, Wis. 54449, USA.
TI - Angiosarcoma of the liver in a rural population: Four cases diagnosed in a 29-month period.
SI - HEEP/77/03476
SO - JAMA (J AM MED ASSOC); 236 (15). 1976 1704-1706
AB - HEEP COPYRIGHT: BIOL ABS. Angiosarcoma of the liver was recently publicized because of its association with polyvinyl chloride (PVC) polymerization workers. Four cases of this rare tumor were observed within a 29 mo. period. There were no

factories that manufacture PVC products in the immediate area, nor were any of the victims ever involved in such manufacturing work. Other factors may be related to this cluster of the disease.

49 AU - ZAEVA GN
AD - Inst. Ind. Hyg. Occup. Dis., Acad. Med. Sci. USSR, Moscow, USSR.
TI - Carcinogenic properties of vinyl chloride: Literature review.
SI - HEEP/77/02385
SO - GIG TR PROF ZABOL; (4). 1976 46-48
AB - HEEP COPYRIGHT: BIOL ABS. Literature data on the carcinogenic properties of vinyl chloride (VC) are presented. Statistics revealed 45 cases of liver angiosarcoma in persons occupationally exposed to VC in 10 countries (USA, Canada, CHSSR (Czechoslovakia), France, Great Britain, Italy, Norway, Rumania, Sweden and FRG (West Germany)). Most reports of these cases were published during the past 7 yr. The mean latent period of tumor development was about 20 yr. The blastomogenic action of VC was also confirmed in experiments in animals with concentrations in a range of 75,000-130 mg/m3. The VC concentration of 130 mg/m3 produced minimal blastomogenic effect. In the USSR the maximum permissible concentration of VC in the production sector is 30 mg/m3. In the USA the hygienic standard is at present reduced from 1300 to 2.6 mg/m3. The results of statistical and experimental investigations justified referring VC to the category of occupational carcinogens.

50 AU - BOLT HM ; KAPPUS H ; BUCHTER A ; BOLT W
AD - Inst. Toxikol., Univ. Wilhelmstr. 56, D-7400 Tuebingen, W. Ger.
TI - Disposition of (1,2-14C) vinyl chloride in the rat.
SI - HEEP/77/01202
SO - ARCH TOXICOL; 35 (3). 1976 153-162
AB - HEEP COPYRIGHT: BIOL ABS. Rats were exposed to the carcinogen (1,2-14C) vinyl chloride in a closed system at initial concentrations below 100 ppm. When the system was occupied by 3 rats, a half-life of vinyl chloride in the system's atmosphere of 1.13 ± 0.12 h was observed. The volume of the system was 10.3 l. Calculation of the clearance of vinyl chloride from the system revealed that about 40% of inspired vinyl chloride is absorbed by lung. Changes in respiration did not influence uptake of vinyl chloride. Uptake of vinyl chloride by the rats was completely blocked by acute pretreatment with potent inhibitors of cytochrome P-450 dependent microsomal drug metabolism (i.e., 35 mg/kg 3-bromophenyl-4(5)-imidazole or 50 mg/kg 6-nitro-1,2,3-benzothiadiazole in 0.6 ml/kg DMSO (dimethylsulfoxide)). A weaker inhibition was observed after SKF 525 A (2-dimethylaminoethyl-2,2-diphenyl valerate) or 5,6-dimethyl-1,2,3-benzothiadiazole (50 mg/kg in 0.6 ml/kg DMSO). Metyrapone did not cause inhibition. Uptake of vinyl chloride was increased by pretreatment with DDT and, to a lesser extent, clotrimazol. No significant stimulation of uptake was observed after pretreatment with phenobarbital, 3-methylcholanthrene, rifampicin or chronic ethanol treatment. Immediately after exposure, highest radioactivity levels were observed in liver and

kidney. The radioactive metabolites of 14C-vinyl chloride were rapidly excreted, largely by the kidneys. Excretion of radioactivity in the urine was 69.4 ± 2.6% within 24 h.

51 AU - WITHEY JR
TI - Pharmacodynamics and uptake of vinyl chloride monomer administered by various routes to rats.
SI - HEEP/76/08961
SO - J TOXICOL ENVIRON HEALTH; 1 (3). 1976 381-394
AB - HEEP COPYRIGHT: BIOL ABS. Finding at least 2-3 ppm and occasionally as much as 10-20 ppm of vinyl chloride monomer in a wide range of foodstuffs prompted concern for a possible human health hazard. The recognition of vinyl chloride as a carcinogen to human in April, 1974, following the discovery of angiosarcoma as the cause of death in at least 25 workers who were engaged in the manufacture of polyvinyl chloride, enhanced this concern with respect to the presence of vinyl chloride monomer in foods. To assess the hazard presented by the oral ingestion of vinyl chloride monomer, rats that were surgically prepared with an indwelling jugular cannula were dosed by intragastric intubation with aqueous solutions containing up to 2.0 mg/ml vinyl chloride. Time-concentration curves were obtained from sequential samples of blood. The uptake of vinyl chloride by this route was extremely rapid. Peak concentrations were achieved less than 10 min after administration of the dose. Elimination from the blood compartment appeared to be biexponential. Studies with the same animal model in a single restraint cage that allowed a head only exposure to concentrations of vinyl chloride up to 7000 ppm in the gas phase showed a similar rapid uptake followed by a plateau blood concentration during several hours of exposure. On removal from the vinyl chloride atmosphere, blood levels fell rapidly to barely detectable concentrations after 2 h. The precise kinetic coefficients that describe the distribution and elimination rates of vinyl chloride from the blood compartment were also determined from the blood concentration data after the administration of an i.v. dose of aqueous or vegetable oil solution.

52 AU - WHELAN J G JR ; CREECH JL ; TAMBURRO CH
TI - Angiographic and radionuclide characteristics of hepatic angiosarcoma found in vinyl chloride workers.
SI - HEEP/76/08407
SO - RADIOLOGY; 118 (3). 1976 549-557
AB - HEEP COPYRIGHT: BIOL ABS. Hepatic angiosarcoma, recently discovered in a large series of vinyl chloride workers, demonstrates characteristic angiographic and radionuclide changes. Tumors exhibiting central hypovascularity with puddling are usually surrounded by a peripheral stain. A negative peripheral defect is demonstrated on the hepatic scan. Healing hepatic infarction secondary to wedged hepatic venography creates a false-positive lesion on angiography similar to angiosarcoma. Splenomegaly and systemic venous hypertension develop in a number of these patients.

53 AU - Shabad LM ; Genin VA
AD - Inst. Eksp. Klin. Onkol., Moscow, USSR
TI - New type of occupational malignant neoplasms induced by vinyl chloride
SI - CA/087/010519M
SO - Gig. Tr. Prof. Zabol.; ISS 7, 1976,41-4
LA - RUS
AB - CBAC COPYRIGHT: CHEM ABS Evidence is found in the literature on vinyl chloride monomer (VVM)-induced liver angiosarcoma, preceded by a complex of specific morphol. changes such as thrombocytopenia, splenomegalia, and hepatomegalia in addn. to portal fibrosis, fibrosis of liver capsule, and signs of acroosteolysis. (75-01-4 Vinyl chloride) Malignant neoplasms including liver hemangiosarcomia, tumors of lymphatic and hematopoietic tissues. Pancreas and bone cancer was the cause of death of 9 out of 24 deceased VCM ex-operators. Exptl. animals exposed to VCM developed subcutaneous and liver angiosarcomas, lymphonia, melanoma skin trichoepithelioma, and transplacentary blastomogenesis. An awareness of the carcinogenic properties of VCM stimulated the revision of the MAC which created the necessity for the soln. of prophylactic and sanitary-technol. problems.

54 AU - Orusev T ; Popovski P ; Bauer S ; Nikolova K
AD - Yugoslavia
TI - Occupational risk in the production of poly(vinyl chloride)
SI - CA/086/194336H
SO - God. Zb. Med. Fak. Skopje; VOL 22,, 1976,33-8
LA - Macedonian
AB - CBAC COPYRIGHT: CHEM ABS Vinyl chloride concns. >75 ppm were measured in the air of a PVC plant. (75-01-4 Vinyl chloride)(9002-86-2 PVC) Examn. of 103 workers revealed 2 cases of enlarged liver, 2 cases of Raynaud syndrome, 2 cases of acroosteolysis, 1 case of lung cancer, and increased incidence of circulatory insufficiencies.

55 AU - Colvin M ; Brundrett RB ; Cowens W ; Jardine I ; Ludlum DB
AD - Sch. Med., Johns Hopkins Univ., Baltimore, Md.
TI - A chemical basis for the antitumor activity of chloroethylnitrosoureas
SI - CA/085/072048Z
SO - Biochem. Pharmacol.; VOL 25, ISS 6, 1976,695-9
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS The aq. decompn. of haloethylnitrosoureas, e.g. 1,3-bis-chloroethyl-1-nitrosurea (I), was studied and related to their antitumor activity. (154-93-8 1,3-Bis-chloroethyl-1-nitrosourea) E.g., I, which has antitumor activity, decomposed to haloethanol, vinyl halide, dihaloethane, and MeCHO, whereas 1-chloroethyl-3,3-dimethyl-1-nitrosourea, which was not toxic to murine L1210 leukemia cells, generated MeCHO but not the other volatile compds. (75-07-0 Acetaldehyde)(59960-30-4

1-Chloroethyl-3,3-dimethyl-1-nitrosourea) In contrast to the disubstituted nitrosoureas, 1-chloroethyl-1-nitrosourea, which has high antitumor activity, did not generate an org. isocyanate on aq. decompn. (2365-30-2 1-Chloroethyl-1-nitrosourea) These data support the hypothesis that the antitumor activity of chloroethylnitrosoureas is due to ethyl carbonium ion (or diazonium precursor) generation.

56 AU - Thomas LB ; Popper H ; Berk PD ; Selikoff I ; Falk H
TI - Vinyl chloride induced liver disease
SI - IPA/75/03331
SO - N. Engl. J. Med.; VOL 292 ISS Jan 2 1975, P17-21, (REF 32)
AB - IPA COPYRIGHT: ASHP Histologic examination of liver tissue (8 autopsy and 18 biopsy specimens) and 4 spleens from 20 workers with vinyl chloride polymerization showed hepatic angiosarcomas in 15. In addition, a peculiar pattern of progressive portal tract, inconspicuous intralobular and conspicuous capsular fibrosis was observed in the 5 workers without angiosarcoma, in all the 7 patients with angiosarcoma from whom tumor free portions of the liver were available, and in 2 tumor free biopsies from patients subsequently found to have angiosarcoma. The fibrosis was accompanied by splenomegaly. Hypertrophy and hyperplasia of both hepatocytes and hepatic and splenic mesenchymal cells were also seen. The histologic similarity to chronic inorganic arsenical poisoning, in which angiosarcomas also occur, and to idiopathic portal hypertension (Banti's syndrome) suggests that the latter syndrome at times results from unknown toxic, possibly environmental, chemicals. APPENDED: Vinyl chloride toxicity, environmental Toxicity, environmental vinyl chloride Polymers vinyl chloride

57 AU - SELINGER M ; KOFF RS
TI - Thorotrast and the liver: A reminder.
SI - HEEP/76/10098
SO - GASTROENTEROLOGY; 68 ((4 PART 1)), 1975 799-803
AB - HEEP COPYRIGHT: BIOL ABS. New insights into carcinogenesis might by gained by further study of Thorotrast-induced human neoplasia. The role of immune mechanisms in the induction of these tumors is uncertain. Thorotrast neoplasms may be RES tumors of multicentric origin. Although exposure to ionizing radiation would appear to be the primary inciting mechanism of Thorotrast carcinogenesis in the liver, no association between liver cell carcinoma or cholangiocarcinoma and atomic bomb exposure was identified in an autopsy series from Hiroshima and Nagasaki (Japan). The possibility of a foreign body or chemical reaction, resembling As-induced malignancy, was also suggested. Although knowledge of vinyl chloride-induced hepatotoxicity is currently limited, the clinical features of vinyl chloride liver disease resemble those associated with Thorotrast. Similarities in latent period and in the development of fibrosis, cirrhosis and angiosarcoma are striking. Whether vinyl chloride-induced carcinogenesis and hepatic injury share features other than clinical expression with Thorotrast remains to be determined.

Regardless of the mechanisms of Thorotrast sequelae, it is apparent that carriers represent a population at risk for the development of liver disease and deserves the attention of hepatologists.

58 AU - BARTSCH H ; MONTESANO R
TI - Mutagenic and carcinogenic effects of vinyl chloride.
SI - HEEP/76/09363
SO - MUTAT RES; 32 (2). 1975 (RECD 1976) 93-114
AB - HEEP COPYRIGHT: BIOL ABS. The carcinogenicity of VCM (vinylchloride monomer) in animals and man and its mutagenic action after metabolic conversion by microsomal enzymes from humans and rodents into electrophilic derivatives further strengthen the establishment of a formal relationship between carcinogenesis and mutagenesis. The screening of a large number of chemicals which are produced on a massive scale and for which a human exposure exists by such mutagenicity assays, in which mammalian and human metabolism are taken into account, would be of great value in the detection of biological hazards. An example of such a chemical is one that is structurally related to VCM 1,1-dichloroethylene (vinylidene chloride), and which is used almost exclusively as a copolymer of VCM in the production of plastic materials. This compound induces point mutation in Salmonella typhimurium strains when assayed in the presence of rat or mouse liver fraction in vitro. Its mutagenic activity is higher than that of VCM. Vinylidene chloride is toxic at high concentrations, and it is carcinogenic in rats. Another chemically related substance, 2-chlorobutadiene (chloroprene), used in the manufacture of synthetic rubber since 1930, was recently suggested as being responsible for an increased incidence of skin and lung cancer in exposed workers, and its activity to induce point mutation in S. typhimurium was demonstrated. The available data indicate that polymerization workers are at a very high risk of angiosarcoma of the liver. Among some 5600 workers currently employed at 36 PVC (polyvinyl chloride) polymerization plants in the U.S.A., 15 cases of angiosarcoma of the liver were reported in 4 of these plants. Nine cases were found in a single plant employing less than 300 workers, and 1 case, a polymerization worker, was exposed to VCM for only 4 yr. Populations at lower levels of exposure are also at risk, as shown by the observation of angiosarcoma of the liver in workers employed in PVC-fabricating plants. The occurrence of few cases of angiosarcoma of the liver among nonoccupationally exposed people and a clustering of cases in a heavily industrialized area could be connected with factory discharge of VCM in the air. Another source of human exposure to VCM is food and beverages packed in PVC containers, since VCM migrates into these commodities. The daily human oral intake was estimated to be less than 100 mug VCM. Since scientific knowledge of chemical carcinogenesis cannot allow the establishment of a safe exposure level for any carcinogen, every effort should be made to prevent exposure and minimize the risk.

59 AU - ZIMMERMANN H ; ECK H
TI - Pathological anatomy of vinyl chloride disease.
SI - HEEP/76/04520
SO - VIRCHOWS ARCH A PATHOL ANAT HISTOL; 368 (1). 1975 51-59
AB - HEEP COPYRIGHT: BIOL ABS. A lethal case of angiosarcoma of the liver is reported. A 38 yr old chemical laboratory assistant was exposed in vinyl chloride (VC) for about 3 1/2 yr. The sarcoma metastasized to many other organs. This case is the 5th reported in the German Federal Republic. In 4 of the cases the patient died. VC concentration at the work place was not measured. Thrombocytopenia observed in about 80% of the VC cases was not seen. There will possibly be further VC-caused tumors in the population. There might be other extrahepatic VC-caused tumors in man, which could be determined by animal experimental investigations.

60 AU - CHABALKO JJ ; FRAUMENI J F JR
TI - Blood-vessel neoplasms in children: Epidemiologic aspects.
SI - HEEP/76/02428
SO - MED PEDIATR ONCOL; 1 (2). 1975 135-142
AB - HEEP COPYRIGHT: BIOL ABS. In a search for etiologic leads to blood vessel neoplasms, 111 death certificates of U.S. children who died from 1960-1968 of angiosarcoma, hemangioendothelioma, and hemangiopericytoma and 127 medical records of similar cases for 12 institutes were examined. The available data provided no leads to environmental agents (vinyl chloride, Thorotrast, As) that can produce vascular liver tumors in adults, but 1 infant, who died from a hepatic tumor, lived within a mile of an industrical source of polyvinyl chloride. About half of the children with hepatic hemangioendotheliomas had associated skin hemangiomas, which may aid in the differential diagnosis of liver tumors in infancy. Hepatic hemangioendotheliomas also predominated in girls, a possible clue to the origin of the tumor. A familial influence was suggested by 1 sibling aggregation of cutaneous hemangioendotheliomas.

61 AU - REIN FR ; HUTH F
TI - Six spontaneous primary malignant vascular tumors of the liver in 30,000 autopsies.
SI - HEEP/76/00073
SO - INT ARCH ARBEITSMED; 34 (4). 1975 237-246
AB - HEEP COPYRIGHT: BIOL ABS. The records of 30,079 autopsies done from 1954-1974 were examined for primary malignant vascular tumors of the liver. Six cases were found (3 males, 3 females, aged between 36 and 76) and histologically reinvestigated. In 4 cases an angiosarcoma was diagnosed, in 1 case a hemangioendothelioma and in another a malignant hemangiopericytoma. Examination of family and case histories, as well as questioning of factory insurance companies and neighbors, led to the conclusion that there was no contact of the subjects with factories producing vinyl chloride. A rate of spontaneous primary malignant vascular tumors of the liver of 0.2% must be

considered with regard to hepatic tumors following contact with industrial toxic substances.

62 AU - BARTSCH H ; MALAVEILLE C ; MONTESANO R
TI - Human, rat and mouse liver-mediated mutagenicity of vinyl chloride in S. typhimurium strains.
SI - HEEP/75/09322
SO - INT J CANCER; 15 (3). 1975 429-437
AB - HEEP COPYRIGHT: BIOL ABS. Exposure of S. typhimurium strains TA 1530, TA 1535 and G-46 to the carcinogen vinyl chloride increased the number of His+ revertants/plate 16, 12 or 5 times over the spontaneous mutation rate. After 6 h of exposure to vinyl chloride, the mutagenic response for TA 1530 strain was enhanced 7-, 4- or 5-fold when fortified postmitochondrial liver fractions from humans, rats or mice were added. The enzyme-mediated vinyl chloride mutagenicity was dependant on an NADPH generating system and the enzyme activity was localized in a liver microsomal fraction; 9,000 x g liver supernatant was 3 times more active than microsomes, while liver cytosol or alcohol dehydrogenase did not affect the mutagenicity. Phenobarbitone pretreatment of rats and mice increased the mutagenic response by 15-40% as compared to untreated controls. The relative mutagenic activities of VCM (vinyl chloride monomer), taking the value from mouse liver as 100, for TA 1530 strain mediated by 9,000 x g tissue fractions were: rat liver 80; mouse and rat kidney, 20 and 16; mouse and rat lung. less than 7; human liver (from 4 biopsy specimens), 170, 64, 70 and 46. Chloroacetaldehyde and chloroacetic acid, a urinary metabolite of VCM, showed toxic effects, while chloroethanol was weakly mutagenic for the TA 1530 strain.

63 AU - Flesch JP ; Rostand RA
AD - Natl. Inst. Occup. Saf. Health, Cincinnati, Ohio
TI - Health hazard evaluation/toxicity determination report H.H.E. 74-94-253, Armstrong Cork Company, Jackson, Mississippi
SI - CA/085/181695D
SO - U. S. NTIS, PB Rep.; ISS PB-249433,, 1975,16 pp.
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS A health hazard existed from exposure to airborne Chrysotile and vinyl chloride in the manuf. of vinyl asbestos floor tiles no findings suggestive of lung cancer were obsd. (12001-29-5 Chrysotile)(75-01-4 Vinyl chloride)

64 AU - Maltoni C ; Lefemine G
AD - Italy
TI - Use of experimental tests in the prediction of environmental oncogenic risk. Vinyl chloride
SI - CA/083/158884Q
SO - Atti Accad. Naz. Lincei, Cl. Sci. Fis., Mat. Nat., Rend.; VOL 56, ISS 3, 1975,412-22
LA - ITA
AB - CBAC COPYRIGHT: CHEM ABS Preliminary results are reported for a comprehensive study of the carcinogenicity of vinyl chloride with

respect to species and age of the test animals, route of administration, dose, duration of exposure, etc. (75-01-4 Vinyl chloride) Vinyl chloride caused carcinomas of Zymbal's glands, nephroblastomas, and hepatic and extrahepatic angiosarcomas in rats and lung tumors, mammary carcinomas, and hepatic angiosarcomas in mice. A dose-response relation was found. These exptl. carcinogenicity bioassays with vinyl chloride are considered highly predictive of effects of industrial exposure of workers. Similar testing of other potentially hazardous industrial substances is advocated.

65 AU - Maltoni C ; Lefemine G
AD - Ist. Oncol., Bologna, Italy
TI - Carcinogenicity bioassays of vinyl chloride. Current results
SI - CA/082/133813G
SO - Ann. N. Y. Acad. Sci.; VOL 246,,, 1975,195-218
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Vinyl chloride (VC) induced tumors in rats, mice, and hamsters, and the spectrum of induced tumors varied from species to species. (75-01-4 Vinyl chloride) E.g., VC produced lung adenomas, mammary carcinomas, liver angiosarcomas and angiomas and skin epithelial tumors in mice, but produced Zymbal gland carcinomas, liver nephroblastomas and angiosarcomas, skin carcinoma, hepatomas and brain neuroblastomas in rats. The strain factor also affected the neoplastic response as reflected by the results obtained from Sprague-Dawley rats and Wistar rats. Two s.c. angiosarcomas were obsd. in the offspring of breeders exposed to VC during pregnancy for 7 days, indicating a transplacental effect. The observation of a few cases of ossifying angiosarcomas suggested a new orientation in the pathogenetic interpretation of acroosteolysis in workers exposed to VC.

66 AU - Monson RR ; Peters JM
TI - Proportional mortality among vinyl chloride workers
SI - IPA/75/00509
SO - Lancet; VOL 2 ISS Aug 17 1974, P397-398, (REF 4)
AB - IPA COPYRIGHT: ASHP In a proportional-mortality analysis of 161 deceased workers in 2 plants using vinyl chloride, a 50% excess of deaths due to all cancer was seen. Specific sites of cancer with the greatest excess included liver and biliary tract, lung, and brain. The excess in fatal cancer was seen mainly in men who died before age 60. Also, there was a trend in time in the ratio of observed to expected deaths: since 1970 over twice as many cancer deaths as expected have occurred. APPENDED: Toxicity, environmental vinyl chloride Vinyl chloride toxicity, environmental Solvents vinyl chloride

67 AU - Lee FI ; Harry DS
TI - Angiosarcoma of the liver in a vinyl chloride worker
SI - IPA/74/04737
SO - Lancet; VOL 1 ISS Jun 29 1974, P1316-1318, (REF 16)
AB - IPA COPYRIGHT: ASHP A 71-year-old man, who had been a process worker in the manufacture of polyvinyl chloride from vinyl chloride monomer for 20 years, died with angiosarcoma of the liver. The evidence appears strong that angiosarcoma of the liver is an occupational tumor and that vinyl chloride is the carcinogen. There is no evidence that the finished polymer carries any risk. APPENDED: Toxicity, environmental polyvinyl chloride Polyvinyl chloride toxicity, environmental Carcinogens vinyl chloride Vinyl chloride carcinogens Toxicity, environmental vinyl chloride

68 AU - EPSTEIN SS
AD - Dep. Pharmacol., Case West. Reserve Univ. Sch. Med., Cleveland, Ohio 44106, USA.
TI - Environmental determinants of human cancer.
SI - HEEP/77/00069
SO - CANCER RES; 34 (10). 1974 2425-2435
AB - HEEP COPYRIGHT: BIOL ABS. The best documented and most significant data on carcinogenesis due to environmental chemicals are those on tobacco. It was suspected for several decades that heavy tobacco smoking is directly and causally related to chronic lung disease, especially cancer. There are also many studies that demonstrate the contributory role of urban air pollution in lung cancer; and numerous classes of chemical carcinogens were identified in polluted urban air. There is an excess of lung cancer deaths in smokers in polluted urban areas in contrast with those living in rural areas. Similar striking regional variations in the occurrence of a wide range of other organ cancers are now well recognized. The high incidence of cancer of the oral cavity in Asia, representing some 35% of all Asiatic cancers, in contrast to 1% of all European cancers, is related to the chewing of betel nuts and tobacco leaves. The high incidence of liver cancer in the Bantu and in Guam may be due to dietary contamination with aflatoxin, and to eating cycad plants, containing azoxyglucoside carcinogens, respectively. The high incidence of gastric cancer in Japan, Iceland and Chile was associated with high dietary intake of fish; suggestions were made implicating nitrosamines, formed by reactions between secondary amines in fish and nitrite preservatives. The high incidence of cancer of the esophagus in Zambians drinking Kachasu spirits, in the Calvados area of France, and in other clearly defined geographic areas may be related to contamination of alcoholic drinks or food with nitrosamines, some of which produce esophageal cancer in experimental animals. Occupational cancers include bladder cancer in the aniline dye and rubber industry, which is induced by such chemicals as 2-naphthylamine, benzidine and 2-aminobiphenyl; 2-nitrobiphenyl induced lung cancer in miners of Colorado, coke oven workers, nitrogen mustard factory

workers in Japan, and in USA workers even briefly exposed to bis(chloromethyl) ether; skin cancer in cutting and shale oil workers; nasal sinus cancer in wood workers; lung cancer and pleural mesotheliomas in insulation workers and in others, such as construction workers, exposed to asbestos; cancer of the pancreas and lymphomas in organic chemists; and angiosarcoma of the liver in workers involved in polymerization processes for the manufacture of polyvinyl chloride.

69 AU - HOLMBERG B ; MOLINA G
TI - The industrial toxicology of vinyl chloride: A review.
SI - HEEP/75/10337
SO - WORK-ENVIRON-HEALTH; 11 (3). 1974 (RECD 1975) 138-144
AB - HEEP COPYRIGHT: BIOL ABS. Acroosteolysis, Raynaud's phenomenon, scleroderma, liver dysfunction and liver angiosarcoma in workers occupationally exposed to vinyl chloride are discussed and toxic and carcinogenic manifestations noted in laboratory animals exposed to vinyl chloride are summarized.

70 AU - FALK H ; CREECH J L JR ; HEATH C W JR ; JOHNSON MN ; KEY MM
TI - Hepatic disease among workers at a vinyl chloride polymerization plant.
SI - HEEP/75/02654
SO - JAMA (J AM MED ASSOC); 230 (1). 1974 59-63
AB - HEEP COPYRIGHT: BIOL ABS. Eleven cases of hepatic disease, including 7 cases of hepatic angiosarcoma were identified to date among men employed at 1 vinyl chloride polymerization plant. The earliest diagnosis was made in Apr. 1964. The 2 most recent cases, both angiosarcoma, were diagnosed in Feb. 1974 as a result of systematic medical screening for liver abnormalities among workers at the plant. Ages at diagnosis have ranged from 36 to 58 yr for the 7 patients with angiosarcoma and from 28 to 56 yr to the 4 patients with nonmalignant disease; durations of employment before diagnosis have ranged from 12 to 28 yr and from 5 to 29 yr. All 11 persons had worked in close and continuous contact with various phases of the vinyl chloride polymerization process. Review of pathologic material suggests the presence in both tumor and nontumor cases of portal fibrosis and atypical sinusoidal lining cells. A direct casual relationship between exposure to vinyl chloride monomer and pathologic findings is postulated.

71 AU - MALTONI C ; LEFEMINE G
TI - Carcinogenicity bioassays of vinyl chloride: I. Research plan and early results.
SI - HEEP/75/01564
SO - ENVIRON RES; 7 (3). 1974 387-405
AB - HEEP COPYRIGHT: BIOL ABS. These investigations are concerned with determining the oncogenic potentialities of vinyl chloride (VC) in experimental animals. The effect of this compound is being studied in relation to various experimental factors, such as route of administration, dose level, length of treatment, species, strain and age of the animals. Preliminary results are

presented. When given by inhalation, VC induces Zymbal gland carcinomas, nephroblastomas and angiosarcomas of the liver and other anatomical sites in rats. In mice, pulmonary adenomas, mammary carcinomas and liver angiosarcomas were noted. A direct relationship was found between dose and length of treatment and neoplastic response.

72 AU - Blyum RA ; Zebenkiene B ; Lutsenko VV ; Liutkiene R
AU - Simkeviciene V
AD - Vilnius, USSR
TI - Some hexamethylenebis(N-nitrosourea) derivatives
SI - CA/087/161408A
SO - Tezisy Dokl. - Vses. Konf. Khimioter. Zlokach. Opukholei, 2nd; 1974,80-2
LA - RUS
AB - CBAC COPYRIGHT: CHEM ABS Four compds. of the general formula (CH2)6[N(NO)CONHR]2 (I) were synthesized and tested for antitumor activity in exptl. animals. The most active was I (R = CH2CH2OH), which inhibited Walker carcinosarcoma by 54.2% and sarcoma 45 by 90.2%. The similar compd. I (R = CH2CH2Cl) inhibited the tumors by 88.6 and 75.7%, resp. Both compds. had the same toxicity, with an LD100 of 500-600 mg/kg, and both lowered spleen wt. and leukocyte no. Compds. I (R = CH2CO2H) and I (R = CH2CO2- +NH3C6H11 were less toxic, but had no antitumor activity. R = CH2CH2OH was also very active against exptl. leukosis. Compds. I (R = CH2CH2OH), I (R = CH2CH2Cl), and hexamethylenebis[N'-(2-chloroethylene)urea] accumulated primarily in the spleen, while none of the compds. accumulated in the brain. (32903-82-5 Hexamethylenebis[N'-(2-chloroethylene)urea])

73 AU - Maltoni C ; Lefemine G ; Chieco P ; Carretti D
AD - Ist. Oncol., Bologna, Italy
TI - Vinyl chloride carcinogenesis. Current results and perspectives
SI - CA/083/091871N
SO - Med. Lav.; VOL 65, ISS 11-12, 1974,421-44
LA - ENG
AB - CBAC COPYRIGHT: CHEM ABS Inhalation of vinyl chloride induced tumors in rats in a dose-dependent manner: at 50-500 ppm it caused angiosarcomas and at 50-250 ppm nephroblastomas. (75-01-4 Vinyl chloride) The induction of the angiosarcomas and nephroblastomas was also dependent on the time of exposure. Subcutaneous angiosarcomas and a Zymbal gland carcinoma occurred in the offspring of rats exposed to vinyl chloride during 7 days of 4 hr daily treatment. Vinyl chloride was carcinogenic also for mice and hamsters.

74 AU - VIOLA PL ; BIGOTTI A ; CAPUTO A
TI - Oncogenic response of rat skin, lungs, and bones to vinyl chloride.
SI - HEEP/73/00108
SO - CANCER RES; 31 (5). 1971 516-522
AB - HEEP COPYRIGHT: BIOL ABS. Rats (Ar/IRE Wistar strain) exposed for 12 mo. to vapors of vinyl chloride developed tumors of the skin, lungs and bones. The cutaneous tumors, which always appeared in the area in which submaxillary and parotid glands are located, were histologically recognized as epidermoid carcinomas, papillomas, and mucoepidermoid carcinomas. The morphological characteristics of lung tumors, which occurred in a lower percentage, were mainly of the adenocarcinoma type, with the exception of a single epidermoid tumor originating from the epithelial covering cells. In a minor number of rats, a large proliferation of cartilaginous tissue diagnosed as osteochondroma developed in the metacarpal and metatarsal regions of the 4 limbs.

* * * * END OF OFFLINE PRINT * * * * *