Chemical file: Vinyl chloride

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Comments Regarding the Agency for Toxic Substances and Disease Registry (ATSDR) Document Entitled "Substance-Specific Applied Research Program Priority Data Needs for Vinyl Chloride" (September, 1992)

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for the

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Vinyl Chloride Panel

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SUMMARY

A report was published by the Agency for Toxic Substances and Disease Registry (ATSDR) which outlined a number of areas in which the agency felt that there were gaps in the available scientific database relating to the compound vinyl chloride monomer (VCM) (ATSDR, 1992). The Chemical Manufacturers Association does not agree with many points made in the ATSDR report and is providing these comments in response.

Vinyl chloride monomer (VCM) is one of the most intensely studied chemicals in use today. The scientific literature contains a wealth of data describing both the short- and the long-term health effects of exposure to this chemical in humans and in a number of species of experimental animals. As such, the potential hazards associated with VCM are well known, yet ATSDR has called for further testing in its report, even though such information would not contribute any significant new information to the toxicological database on VCM.

The report prepared by ATSDR does not adequately acknowledge that the potential risk to humans of a chemical is a factor of both its hazard potential and the level of exposure. A chemical, regardless of its toxicological potential to affect the health of individuals in the vicinity of hazardous waste site, cannot pose a health hazard if there is no or negligible exposure. It is the level of potential exposure to VCM in the vicinity of hazardous waste sites that should be the focus of any future data gathering, and not items such as additional nonclinical testing, epidemiological studies, development of methods to mitigate toxicity, or the creation of a registry of exposed persons around such sites. Furthermore, it is not evident from the ATSDR document that there is recognition that VCM that may be present at waste sites is not the result of disposed of VCM itself or even discarded polyvinyl chloride materials, but rather is the result of degradation of commonly used solvents. Any attempts at reducing the potential risks associated with living near a hazardous waste site should be addressed through better waste disposal practices.

1.0 INTRODUCTION

The Agency for Toxic Substances and Disease Registry (ATSDR) released a document Entitled "Substance-Specific Applied Research Program Priority Data Needs for Vinyl Chloride" (ATSDR, 1992). The focus of this document was exposure from hazardous waste sites, vinyl chloride monomer (VCM) is one of the most intensely studies chemicals in use today, with the potential risks of this chemical well known, yet the ATSDR document does not accurately reflect this. The Chemical Manufacturers Association herein provides its comments regarding points made in the ATSDR document in order to clarify the issues.

2.0 SPECIFIC COMMENTS - DATA NEEDS

In order to respond to the ATSDR report regarding data needs, we have used the ATSDR framework for the sake of organization of these comments.

2.1 Exposure to VCM

2.1.1 Exposure Levels - Environmental Media

The purpose of Section III.A.1.c.i in the ATSDR report was to determine if adequate data on the levels of VCM in ambient and contaminated environments are available for the purposes of conducting meaningful follow-up exposure and health studies. The document provides a series of numbers describing concentrations of VCM detected in air and water media. It does not, however, provide the reader with a sense of what these values actually mean with respect to potential risks, and then concludes that there is a need for such data in environmental media at hazardous waste sites.

There is a considerable amount of data available concerning VCM concentrations in environmental media around PVC production facilities, and also concentrations of VCM in the indoor work environment at these facilities. In the work place, the data that are available are an excellent source of information with respect to determining the effects of VCM on humans

where the exposure to VCM has been documented. This, in turn, allows a more controlled way of determining potential risk to humans, as the exposure has been accurately defined. Such a situation does not exist with respect to hazardous waste sites, as there would be no indication of exposure to the multitude of other compounds that would confound any follow-up epidemiological studies or analyses.

Given the fact that the potential risk from VCM around hazardous waste sites is dependent upon the level of exposure, it is worth reviewing the available data from industrial exposure for the purpose of putting relevant exposure into perspective.

2.1.1.1 VCM in Workplace Air

Concentrations of VCM in the workplace prior to the 1960s were greater than 100 ppm and decreased to values less than 100 ppm between the 1960s and mid-1970s, then decreased again to an upper limit of 5 ppm [8 hour, time-weighted-average (TWA)] by 1975 (Doll, 1988; ACGIH, 1991). The current OSHA workplace standard in the United States is 1 ppm (8 hour TWA) with a 5 ppm short-term exposure limit (STEL) (29 CFR 1910.1017).

In 1988, the concentrations of VCM (8 hour TWA based on individual personnel monitoring) in the work environment ranged from approximately <0.25 to 10.5 mg/m^3 (<0.1 to 4.1 ppm) in four PVC resin production facilities in the United States. Reactor operators, loading personnel and laboratory technicians showed the greatest potential exposures for 8 hour exposures. TWA air concentrations ranged from 0.5 to 11 mg/m^3 (0.2 to 4.1 ppm); these air concentrations had decreased to 0.5 to 2 mg/m^3 (0.2 to 0.77 ppm) in 1992. In 1990, one facility reported 8 hour TWA concentrations in air for instrument technicians and process operators of 35 and 26.5 mg/m^3 (13.5 and 10.3 ppm), respectively. By 1992 (January to September data only), the work-place concentrations in these facilities had decreased to a range of approximately <0.25 to 2 mg/m^3 (<0.1 to 0.8 ppm). These data represent the greatest concentrations of VCM in air reported for these four facilities over the five year period 1988 through 1992 (Vinyl Institute, personal communication). Localized releases of VCM to the natural environment can

occur around production and manufacturing facilities; therefore, the concentrations of VCM are highest near such facilities.

2.1.1.2 VCM in Environmental Emissions from Production Facilities

Decreases in concentrations of VCM in the work environment discussed above would also be indicative of corresponding decreases in environmental releases from production/manufacturing facilities. VCM has been measured in air around suspected "hot spots" (*i.e.*, in areas near production and manufacturing facilities) in the United States. Prior to the implementation of VCM emission regulations in 1978, the average air concentrations of VCM at production facilities in the United States was 0.04 mg/m^3 (0.017 ppm) (IARC, 1979). In Houston, Texas, where large quantities of VCM are produced, air concentrations ranged from 0.008 mg/m^3 (0.003 ppm) to peak values of 3.2 mg/m^3 (1.2 ppm) (Gordon and Meeks, 1977). In Long Beach, California, ambient air concentrations of VCM near two VCM plants ranged from 0.3 to 8.8 mg/m^3 (0.1 to 3.4 ppm) (National Field Investigations Center, 1974). However, within approximately one kilometer of VCM production/manufacturing facilities, reported air concentrations of VCM ranged from approximately 0.03 to 0.1 mg/m^3 (0.01 to 0.04 ppm) (EPA, 1975b; Baxter *et al.*, 1977). More recent information based on sampling near production/manufacturing facilities since standards for the work environment were reduced to about 13 mg/m^3 (5 ppm) in 1975, showed that air concentrations of VCM were near the analytical detection limit (about 0.013 mg/m^3 or 0.005 ppm) in three out of five British plants. For two other facilities, the VCM air concentrations were approximately 0.05 mg/m^3 (0.02 ppm) at a location 100 m outside the facility boundary, and 0.2 mg/m^3 (0.09 ppm) just inside the boundary fence (Turner *et al.*, 1984).

2.1.1.3 Risk from VCM in Workplace Air

The best available epidemiological data regarding exposure to VCM were critically reviewed by Sir Richard Doll (Doll, 1988). This review clearly illustrated the current understanding that the potential risk associated with VCM is a factor of the level of exposure, with there being no significant risk to humans below certain levels. The review, which incorporated well-

documented levels of exposure of humans to VCM had two major conclusions: (i) Apart from liver cancer, VCM/PVC workers exposed between the 1940s/1950s and mid-1970s did not have unusual hazards of accident or disease, and (ii) workers exposed to VCM concentrations of "several hundred parts per million or more" clearly showed an increased risk of contracting angiosarcoma of the liver, normally an extremely rare disease (annual incidence of 1 to 2 x 10^{-7} in the general population; Byren and Holmberg, 1975).

Doll (1988) concluded that it was "difficult to decide whether vinyl chloride produces a risk of developing cancer other than angiosarcoma of the liver which might be small compared to the risks produced by nonoccupational causes, at sites other than the liver" (Doll, 1988). He also concluded that there was no evidence to support the association between exposure to VCM and any other digestive tract cancer. Doll's review did not support a significant association between VCM exposure and the risk of brain cancer when the combined data from four major epidemiological studies were analyzed (Doll, 1988). An apparent excess risk of brain cancer among VCM workers in the United States, reported in a study conducted by Wong *et al.* (1991), was subsequently attributed to chance or diagnostic bias by the authors (Wong and Whorton, 1993). With respect to the association of exposure to VCM and lung cancer, Doll (1988) concluded that a small hazard may have existed when occupational exposures to VCM were extreme, but that the study data did not conclusively demonstrate this risk and that the increased risk would in any case be negligible at the current small exposures to VCM.

2.1.1.4 Risk from Environmental Emissions of VCM in Air

In his review, Doll concluded that the minute exposures that would result from emissions escaping from VCM facilities must cause comparably minute risks to the general public. The concentrations of VCM measured near VCM/PVC production/manufacturing facilities are in the order of 0.01 to 0.04 ppm (EPA, 1975b; Baxter *et al.*, 1977), or some 10,000-fold less than the "several hundred parts per million or more " exposures that resulted in measurable occupational hazards. Therefore, an increased risk of cancer to the general public could not possibly be detected, with the possible exception of an increased risk of angiosarcoma of the liver. Any inference that angiosarcoma incidence in the general population is related to VCM exposure,

however, could be misleading because angiosarcoma may also be caused by thorium dioxide and arsenic in pesticides and by certain medicines (Doll, 1988).

Doll (1988) also concluded that there may have been a minute hazard to the general public from the VCM concentrations historically observed around manufacturing facilities. However, the concentrations of VCM around production facilities has decreased substantially since the 1970s. VCM air concentrations within a few hundred meters of VCM areas were below analytical detection limits (< 0.005 ppm) for three of five facilities in the United Kingdom, and the concentrations for the other two facilities were about 0.02 ppm (100 m outside the boundary fence), and 0.09 ppm (just inside the boundary fence). However, accidents and production start-ups were associated with higher concentrations (Turner *et al.*, 1984). Based on this evidence, Doll (1988) concluded that "according to any reasonable criterion, the hazard to the general public (if there is any at all) must be negligible."

2.1.1.5 VCM in Water

Vinyl chloride also has been measured in both groundwater and drinking water in the United States. The greatest concentration of VCM measured in drinking water was 0.01 mg/L near a production facility (Safe Drinking Water Committee, 1977; IARC, 1979). Vinyl chloride monomer has also been reported in groundwater in the United States. Measurable levels in California wells averaged 0.02 mg/L and were as high as 0.023 mg/L (Kizer, 1986). In the Los Angeles area, groundwater contained less than 0.001 mg/L of VCM (Baird *et al.*, 1983), while in non-specified areas of Nebraska and California groundwater concentrations ranged from 0.75 to 0.023 mg/L (Goodenkauf and Atkinson, 1986; CSDHS, 1990).

As described in the preceding sections, there are good data available from which to predict potential risks of individuals from VCM. In the opinion of the Chemical Manufacturers Association, the ATSDR appears to not be utilizing the exposure-response data of VCM that already are available for humans.

2.1.2 Exposure Levels - Humans

Section III.A.1.c.ii of the ATSDR report states that there is a lack of data regarding levels of vinyl chloride in body tissues or fluids. ATSDR considers these data important for conducting meaningful follow-up exposure and health studies with individuals exposed to VCM and points out that there is no validated biomarker of VCM exposure currently available from which to use for the purposes of dosimetry. The development of the database as described is considered by the Chemical Manufacturers Association to be unnecessary and would appear to be a waste of resources.

ATSDR is correct in its view that thiodiglycolic acid, a major metabolite of VCM, is of limited value for the monitoring of VCM exposure due to confounding factors such as variable metabolism between individuals, influences of disease states, and the fact that this metabolite is not unique to VCM exposure. There is currently work going on that involves biomarkers of exposure (Ciroussel *et al.*, 1990; Swenberg *et al.*, 1992), although it is not yet at the stage where it is a reliable predictor of quantitative exposure. Any type of methodology that ATSDR puts forward to monitor human exposure to VCM must be specific and it must be quantitative. There is no mention in the document that ATSDR acknowledges the work that is currently being undertaken in this area.

In addition, ATSDR considers that modeling cannot reliably predict levels of VCM in human tissues for the purposes of further studies, yet it does not give an explanation for this statement. As indicated in the report, there is currently an effort underway at ATSDR to examine data from 245 National Priorities List (NPL) sites at which VCM has been found. This database, when completed, will include the concentrations in on-site and off-site media, the sizes of the potentially exposed populations, and an indication of relevant exposure routes. From these concentrations determined by ATSDR, it would be possible to predict potential exposure to VCM and assess the risk, if any, to persons nearby without the need to (a) develop and validate methods for quantifying exposure and (b) actually apply these methods to untold numbers of individuals living within predetermined distances from hazardous waste sites, as is alluded to by ATSDR.

As discussed above, the current epidemiological information that was critically reviewed by Doll (1988) has indicated clearly that for individuals living around production facilities, where VCM concentrations in ambient air have ranged from approximately 0.005 to 0.09 ppm since the introduction of standards, the hazard is negligible. Such a conclusion is based upon well documented exposure in industrial workers, where concomitant exposure to other agents/chemicals have been addressed in a way not possible in the recommendation of ATSDR.

2.2 Registry of Exposed Persons

The ATSDR document states that a registry of individuals exposed to VCM in the environment would provide an important reference tool to aid in assessing long-term health consequences of such exposure (Section III.2.a). In the opinion of the Chemical Manufacturers Association, it is believed that no significant information would be gleaned regarding the human health effects of VCM, from the setting up of such a registry, that is not already available from the numerous epidemiological reports available that have been based upon occupational exposure to this chemical (see review by Doll, 1988). Such data regarding occupational exposure to VCM also has the advantage that concomitant exposure to other chemicals is minimized when compared to exposure via a hazardous waste site, where it may not be possible or economically feasible to analyze the various media for all possible chemicals that could influence the health of humans in areas adjacent to hazardous waste sites. To open a registry, as ATSDR is recommending, would be prohibitively time-consuming and expensive, and, in the opinion of the Chemical Manufacturers Association, would not provide any significant new information. It would have to take into account and pay considerable attention to case histories, the long-term exposure history, and confounding factors such as smoking. Interestingly, VCM has itself been found in tobacco smoke (Hoffmann *et al.*, 1976). Even if establishment of a registry was undertaken, the fact that it would be impossible to quantitatively document the past exposure to VCM from hazardous waste sites and to consider all the possible confounding factors would make this information of little practical use.

As indicated previously, even in the case of industrial workers exposed, for all practical purposes to pure VCM, there are levels of exposure that have been found to have no significant

effects upon the health of the individuals (Doll, 1988). Only angiosarcoma of the liver has been definitively linked to VCM exposure, except possibly for a possible risk of lung cancer when exposure has been large (Doll, 1988). Based upon these data, even if ATSDR were able to solicit the cooperation of all the people potentially exposed to VCM from living near hazardous waste sites, and had unlimited access to funding, no new information would be generated regarding the potential hazards of VCM. Also, it should be noted that when considering the potential risk of VCM, the production, use, and transportation of VCM provide the more critical areas for monitoring of exposure as compared to disposal sites.

2.3 Toxicity of VCM

2.3.1 Acute Exposure

In Section III.B.1.a of the ATSDR report, it is stated that acute duration nonclinical studies are a priority data need in order to identify target organs and levels of exposure which present a significant risk to human health following acute exposure. It is unclear what the relevance of conducting such a study(ies) would be, considering that exposure to VCM at or near a waste disposal site would be expected to be long-term at low concentrations. The effects of longer term exposure in laboratory animals has been previously reviewed by ATSDR in its toxicological profiles on VCM (ATSDR, 1989; ATSDR, 1993).

It is typical for acute exposure studies to essentially measure lethality in the test animal, while it seems to be the intent of ATSDR to obtain data regarding more subtle endpoints and no-effect doses for effects that are characteristically obtained from longer term investigations. The Chemical Manufacturers Association cannot see what new or additional data, generated as a result of this proposed data need, would add to what is currently available in the literature.

2.3.2 Reproductive and Developmental Toxicity

Animal and human studies with VCM do not indicate effects upon reproduction and/or development, effects suggested in the ATSDR report (Sections III.B.1.e and f). This lack of

potential effects of VCM on human offspring was the focus of a 1987 report prepared by the Vinyl Institute and included with these comments as Appendix A (Vinyl Institute, 1987). The ATSDR seems to have incorrectly confused the effects of maternal toxicity at high doses of VCM with reproductive and/or developmental effects in its report. This is particularly evident in ATSDR's review of the studies reported by John *et al.* (1977; 1981), where groups of pregnant rats, mice and rabbits were exposed via inhalation to VCM at concentrations of 0, 50, 500 or 2,500 ppm for seven hours per day during the critical period of organogenesis. Although the high levels of VCM caused maternal toxicity, there was no significant embryonal or fetal toxicity observed nor were there any teratogenic effects produced in the offspring.

2.4 Biomarkers

Biomarkers, in effect, relate directly to other areas discussed in the ATSDR report and in these comments; namely the monitoring of exposure to VCM and the creation of a registry of exposed persons. These items would require sensitive and specific methods of quantitatively documenting exposure to VCM. Such a biomarker would essentially provide dosimetry data for a particular individual, although the use of such data in comparisons to potential risks would have to be exhaustively validated in order for them to be of any potential use. The Chemical Manufacturers Association believes that information related to adducts formed by the interaction between industrial chemicals and macromolecules is important with respect to exposure and the assessment of risk, and currently supports work in this area for a number of compounds. There is a considerable amount of work presently being conducted with VCM related to adduct formation, adduct stability, and the effects of these upon specific genes (Jacobsen and Humayun, 1989; Ciroussel *et al.*1990; Swenberg *et al.*, 1992). As such, the Chemical Manufacturers Association feels that the development of suitable biomarkers for VCM exposure and for subsequent risk assessment is currently being addressed.

2.5 Clinical Methods of Mitigating Toxicity

These comments on clinical methods made by ATSDR (Section III.B.2.d) do not provide meaningful guidance as they could be taken to mean everything from the development of early

diagnostic methods to finding a cure for angiosarcoma of the liver. Essentially, toxicity due to VCM could be reduced or eliminated altogether through reduction in exposure. Such results have been clearly demonstrated for industrial exposure (see comment 2.1.1). The reduction or elimination of exposure of individuals to VCM near NPL sites is a factor of better waste management practices and monitoring by federal authorities.

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Vinyl Chloride and Polyvinyl Chloride: Toxicology
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SAMPLE CITATION

Title--------Changes of the Organs of Locomotion in Adult Alcoholism.

Accession----80-01 16865
Number

Author-------Szanto, D.

Citation-----Magy. Radiol., 31(3), 133-139 (1979) Language - German, English, Hungarian, Russian Affiliation- (Egyesitett Tudokorhaz-Gondozointezet, Pf. 175, 3501 Miskole, Hungary) Type- Journal Article: Orig. Research

Abstract-----The X-ray pathology of the limbs of 7 patients with chronic alconolism is described.

SAMPLE SUBJECT INDEX ENTRY

Keyword------------------------Locomotion

Citation number-------------5

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Combustion of Plastics and Elastomers (Jan 76 - Present)

USG/NTIS
ORDER NUMBER PB93-877652/RPS

The bibliography contains citations concerning combustion and combustion products of plastics and elastomers. Topics include combustion chemistry, fire safety, toxic gases, burning rate, and techniques and additives to make plastics and elastomers fire resistant or less hazardous. (Contains 250 citations fully indexed with a title list.)

Sister Chromatid Exchange Analysis to Monitor Genotoxic Chemicals (Jan 81 - Present)

POLLUTION ABSTRACTS
ORDER NUMBER PB92-853563/RPS

The bibliography contains citations concerning the use of the sister chromatid exchange (SCE) analysis for toxicological studies. SCE analysis is a very sensitive measure of genotoxic damage to chromosomes. SCE toxicological studies analyzing ionizing radiation, chromium compounds, styrene, paint thinner, mercury, cigarette smoke, coal dust, fuel oil, insecticides, ethylene oxide, diesel exhaust, and polychlorinated biphenyls are discussed. SCE studies using both human and animal tissue cultures are described. (Contains a minimum of 182 citations fully indexed with a title list.)

Polymeric Materials Combustion: Toxicity Hazards and Legal Aspects (Jan 73 - Present)

Rubber & Plastics Research Abstracts
ORDER NUMBER PB90-855578/RPS

This bibliography contains citations concerning toxicity hazards and legal aspects of polymeric materials combustion in building, electrical and electronic applications. Flammability assessment, flame retardant additives, and toxicity standards of polymeric materials are discussed. Regulations and legislation on polymer flammability are presented. Health hazards caused by toxic gases from polymeric materials combustion are considered. (Contains a minimum of 238 citations fully indexed with a title list.)

Toxicity: Polymeric Materials in Food-Contact Applications (Jan 77 - Present)

Rubber & Plastics Research Abstracts
ORDER NUMBER PB89-871214/RPS

This bibliography contains citations concerning toxicity investigations of polymeric materials in food-contact applications. Polymeric food packaging materials and regulations are discussed. Toxicity testing, polymeric equipment in food processing, and the use of additives in food packaging are included. Discussions also include coating materials for food containers and pigments for food packaging films.(Contains 250 citations fully indexed with a title list.)

Sister Chromatid Exchange Analysis to Monitor Genotoxic Chemicals (Jan 81 - Present)

POLLUTION ABSTRACTS
ORDER NUMBER PB93-863009/RPS

The bibliography contains citations concerning the use of the sister chromatid exchange (SCE) analysis for toxicological studies. SCE analysis are very sensitive measures of genotoxic damage to chromosomes. SCE toxicological studies analyzing ionizing radiation, chromium compounds, styrene, paint thinner, mercury, cigarette smoke, coal dust, fuel oil, insecticides, ethylene oxide, diesel exhaust, and polychlorinated biphenyls are discussed. SCE studies using both human and animal tissue cultures are described. (Contains a minimum of 191 citations fully indexed with a title list.)

BIBLIOGRAPHIC INFORMATION

PB93-878361

Vinyl Chloride and Polyvinyl Chloride: Toxicology (Jan 82 - Present)

Citations from the Life Sciences Collection Database

Jul 93

National Technical Information Service, Springfield, VA

Report Period Covered: Jan 82 - Present

Supersedes PB92-854330

The bibliography contains citations concerning the toxicity of vinyl chloride and polyvinyl chloride following short- and long-term exposure. The citations explore how these compounds are metabolized and consider their carcinogenic and teratogenetic potential. Methodologies to quantitate their presence in atmospheric dust and body tissues are discussed. Occupational hazards are also noted. (Contains 139 citations fully indexed with a title list.)

Price Code: PC NO1 MF NO1

TITLE LIST

		TITLE
1.	NDN 122-0121-4796-4:	Exposures to polyvinyl chloride, methyl ketone and other chemicals: The pulmonary and non-pulmonary effect.
2.	NDN 122-0121-2575-0:	Contrasting effects of 1,1,1-trichloroethane on (super(14)C)vinyl chloride metabolism and activation in hepatic microsomes from phenobarbital- and isoniazid-treated rats.
3.	NDN 122-0120-2796-0:	Toxicity of polyvinylchloride plastizoles of C, M, P brands for manufacturing medical products.
4.	NDN 122-0118-0265-0:	Mortality and cancer incidence among PVC-processing workers in Sweden.
5.	NDN 122-0116-1625-7:	Migration of vinyl chloride into PVC-bottled drinking-water assessed by gas chromatography-mass spectrometry.
6.	NDN 122-0115-4786-7:	An industry-wide epidemiologic study of vinyl chloride workers 1942-1982.
7.	NDN 122-0113-3432-0:	Pulmonary effects of polyvinyl chloride dust exposure on compounding workers.
8.	NDN 122-0111-3502-4:	A collaborative study of cancer incidence and mortality among vinyl chloride workers.
9.	NDN 122-0110-3529-7:	Liver and biliary tract cancer among chemical workers.
10.	NDN 122-0110-3038-0:	Mortality and cancer morbidity in workers exposed to low levels of vinyl chloride monomer at a polyvinyl chloride processing plant.
11.	NDN 122-0109-3022-9:	Etheno adducts formed in DNA of vinyl chloride-exposed rats are highly persistent in liver.
12.	NDN 122-0109-1959-3:	Exposure to vinyl chloride monomer: Results of a cohort study after a seven year follow up.
13.	NDN 122-0108-4562-7:	The persistence of sister-chromatid exchange frequencies in men occupationally exposed to vinyl chloride monomer.
14.	NDN 122-0106-6126-7:	Activation of Ki-ras gene by point mutation in human liver angiosarcoma associated with vinyl chloride exposure.
15.	NDN 122-0105-2135-4:	Lifetime (149-week) oral carcinogenicity study of vinyl chloride in rats.
16.	NDN 122-0101-5329-8:	Pathobiochemical response of tracheobronchial lymph nodes following intratracheal instillation of polyvinylchloride dust in rats.
17.	NDN 122-0100-2684-7:	Vinyl chloride-induced DNA adducts. II: Formation and persistence of 7-(2'-oxoethyl)guanine and N super(2),3-ethenoguanine in rat tissue DNA.
18.	NDN 122-0098-2219-6:	Sister chromatid exchanges, proliferating rate index, and micronuclei in biomonitoring of internal exposure to vinyl chloride monomer in plastic industry workers.
19.	NDN 122-0097-5959-0:	Mutagenicity of vinyl chloride in man: Comparison of chromosome aberrations with micronucleus and sister-chromatid exchange frequencies.
20.	NDN 122-0097-2585-3:	Tissue reaction to intraperitoneal polymer implants: Species difference and effects of corticoid and doxorubicin.
21.	NDN 122-0094-6415-2:	Persistent liver dysfunction among workers at a vinyl chloride monomer polymerization plant.

22. NDN 122-0093-7792-9: Epithelioid hemangioendothelioma of the liver following contact with vinyl chloride. Recurrence after orthotopic liver transplantation.

23. NDN 122-0091-7762-0: Rapid analysis of dibutyltin compounds and tricresyl phosphate in polyvinyl chloride (PVC) by thin layer chromatography.

24. NDN 122-0090-9368-0: Cot mattress biodeterioration and SIDS.

25. NDN 122-0088-6956-9: 1,N super(6)-Ethenoadenosine formation, mutagenicity and murine tumor induction as indicators of the generation of an electrophilic epoxide metabolite of the closely related carcinogens ethyl carbamate (urethane) and vinyl carbamate.

26. NDN 122-0085-7170-2: Nucleophilic selectivity as a determinant of carcinogenic potency (TD sub(50)) in rodents: A comparison of mono- and bi-functional alkylating agents and vinyl chloride metabolites.

27. NDN 122-0085-2228-4: Occupational asthma due to unheated polyvinylchloride resin dust.

28. NDN 122-0084-4487-0: Effects of vinyl chloride on liver function of exposed workers, evaluated by measurements of plasma clearance of the super(99m)Tc-N-2,4-dimethylacetanilido-iminodiacetate complex.

29. NDN 122-0083-2743-8: Small airways function in workers processing polyvinyl chloride.

30. NDN 122-0082-3291-9: Central nervous system malformations in relation to two polyvinyl chloride production facilities.

31. NDN 122-0081-2180-0: Comparison of potency of human carcinogens: Vinyl chloride, chloromethylmethyl ether and bis(chloromethyl)ether.

32. NDN 122-0080-0176-4: Update to vinyl chloride mortality study.

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34. NDN 122-0076-8840-3: Cohort and case-control analyses of workers exposed to vinyl chloride: An update.

35. NDN 122-0073-2887-3: Immunochemical profiles of workers differing in the degree of occupational exposure to vinyl chloride.

36. NDN 122-0070-9669-0: Carcinogenicity of vinyl chloride in Sprague-Dawley rats after prenatal and postnatal exposure.

37. NDN 122-0069-7930-0: Factors of humoral resistance in workers exposed to vinyl chloride with a view to smoking habits.

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46. NDN 122-0055-1703-4: The vinyl chloride-derived nucleoside, N super(2),3-ethenoguanosine, is a highly efficient mutagen in transcription.

47. NDN 122-0054-4295-2: Utilization of 1, N super(6)-etheno-2'-deoxyadenosine 5'-triphosphate during DNA synthesis on natural templates, catalyzed by DNA polymerase I of Escherichia coli).

48. NDN 122-0054-4259-9: In vitro studies on the metabolism and covalent binding of (super(14)C)1,1-dichloroethylene by mouse liver, kidney and lung.

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50. NDN 122-0049-1365-5: Quantitative histochemistry of benzaldehyde dehydrogenase in hepatocellular carcinomas of vinyl chloride-treated rats.

51. NDN 122-0048-5695-7: Two stages of cancerogenesis induced by implantation of foreign objects.

52. NDN 122-0048-5464-0: Phthalate ester exposure-air levels and health of workers processing polyvinylchloride.

53. NDN 122-0047-4682-9: Statistical modeling of animal bioassay data with variable dosing regimens: Example--vinyl chloride.

54. NDN 122-0046-4902-2: The value of some cytoenzymochemical investigations of the leukocytes and platelets in estimating the effects of occupational exposure to benzene, vinyl chloride and carbon disulphide.

55. NDN 122-0044-4956-2: Application of the "filter model" to a risk assessment for vinyl chloride.

56. NDN 122-0042-0609-4: Effect of vinyl chloride on testis in rats.

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61. NDN 122-0036-1252-0: Bronchitis in relation to work.

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63. NDN 122-0036-0680-5: Pulmonary function and respiratory symptoms in polyvinylchloride fabrication workers.

64. NDN 122-0030-7252-5: Vinylchloride induced hepatic angiosarcoma.

65. NDN 122-0030-6718-9: Epidemiological study of the lung function of workers at a factory manufacturing polyvinylchloride.

66. NDN 122-0029-8109-8: Two cases of liver angiosarcoma among polyvinyl chloride (PVC) extruders of an Italian factory producing PVC bags and other containers.

67. NDN 122-0029-6804-5: Assessment of mutagenic efficiency of two carcinogen-modified nucleosides, 1,N super(6)-ethenodeoxyadenosine and O super(4)-methyldeoxythymidine, using polymerases of varying fidelity.

68. NDN 122-0028-9303-3: Preventive measures against occupational hazards in the PVC

production industry.

69. NDN 122-0028-9298-3: Occupational hazards in the VC-PVC industry.

70. NDN 122-0028-9289-2: Trends in cancer mortality among workers in the synthetic polymers industry.

71. NDN 122-0028-9276-4: Toxicity of the components of poly(vinylchloride) polymers additives.

72. NDN 122-0028-9258-2: The toxicology of monomers of the polyvinyl plastic series.

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89. NDN 122-0013-7872-6: Mitochondrial changes in hepatocytes of rats chronically exposed to vinyl chloride and ethanol.

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91. NDN 122-0013-7731-0: Cause-specific mortality study on VCM workers.

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93. NDN 122-0011-8845-7: Investigations on the correlation between vinyl chloride (VCM)-uptake and excretion of its metabolites by 15

VCM-exposed workers: II. Measurements of the urinary excretion of the VCM-metabolite thiodiglycolic acid.

94. NDN 122-0011-8764-7: Effects on the liver of chemicals encountered in the workplace.

95. NDN 122-0011-2486-8: Cytogenetic effects of epoxy, phenolformaldehyde and polyvinylchloride resins in man.

96. NDN 122-0010-3562-8: Raynaud's Phenomenon Caused by Vinyl Chloride. Raynaud-Phaenomen Durch Vinylchlorid.

97. NDN 122-0010-0737-2: Plasticizer Migration From Polyvinyl Chloride Film to Solvents and Foods.

98. NDN 122-0010-0725-6: The Effect of Repeated Vinyl Chloride Exposure on Rat Hepatic Metabolizing Enzymes.

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100. NDN 122-0009-9469-7: Progression of Vinyl Chloride Induced Hepatic Fibrosis to Angiosarcoma of the Liver.

101. NDN 122-0009-9427-2: Angiographic Study of Digital Arteries in Workers Exposed to Vinyl Chloride.

102. NDN 122-0009-8920-3: Polyvinyl Chloride Wire Insulation Decomposition II: Consideration of Long Term Health Effects From Chlorinated Hydrocarbons.

103. NDN 122-0008-0888-9: Review of Epidemiologic Study Results of Vinyl Chloride-Related Compounds.

104. NDN 122-0008-0882-8: Review of Experimental Carcinogenesis by Compounds Related to Vinyl Chloride.

105. NDN 122-0008-0877-4: Angiosarcoma of the Liver: A Signal Lesion of Vinyl Chloride Exposure.

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110. NDN 122-0008-0838-5: Review of Pulmonary Effects of Poly(Vinyl Chloride) and Vinyl Chloride Exposure.

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112. NDN 122-0008-0763-0: Epidemiological Study of Pneumoconiosis in the Italian Poly(Vinyl Chloride) Industry.

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115. NDN 122-0008-0734-4: Poly(Vinyl Chloride) Processes and Products.

116. NDN 122-0008-0721-6: Effectiveness of Federally Required Medical Laboratory Screening in the Detection of Chemical Liver Injury.

117. NDN 122-0008-0713-7: Epidemiology of Hepatic Angiosarcoma in the United States: 1964-1974.

118. NDN 122-0008-0708-3: Epidemiologic Study of Vinyl Chloride Workers: Mortality Through December 31, 1972.

119. NDN 122-0008-0705-8: German Investigations on Morbidity and Mortality of Workers Exposed to Vinyl Chloride.

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121. NDN 122-0008-0698-4: Results of Sputum Cytology Among Workers Exposed to Vinyl Chloride Monomer and to Poly(Vinyl Chloride).

122. NDN 122-0008-0693-5: Preliminary Observations of the Effect of Inhalation of PVC in Man and Experimental Animals.

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125. NDN 122-0008-0675-3: Effect of Ethanol on Vinyl Chloride Carcinogenesis.

126. NDN 122-0008-0667-4: Effects of Aging on the Induction of Angiosarcoma.

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130. NDN 122-0007-9381-3: Detection of N super(2),3-Ethenoguanine in DNA After Treatment With Chloroacetaldehyde in vitro.

131. NDN 122-0006-1490-6: Polyvinyl Chloride Pulmonary Disease.

132. NDN 122-0006-1489-0: Power Considerations in Epidemiologic Studies of Vinyl Chloride Workers.

133. NDN 122-0005-3386-4: Follow-Up Study on the Carcinogenicity of Vinyl Chloride and Vinylidene Chloride in Rats and Mice: Tumor Incidence and Mortality Subsequent to Exposure.

134. NDN 122-0003-5725-9: Evidence for Endothelial Cell Origin of Vinyl Chloride-Induced Hepatic Angiosarcoma.

135. NDN 122-0003-5475-1: Neurological Changes in Vinyl Chloride-Exposed Workers.

136. NDN 122-0003-0693-8: Ultrastructure of Hepatic Angiosarcoma in Rats Induced by Vinyl Chloride.

137. NDN 122-0003-0663-0: Cancer Mortality of a Group of Canadian Workers Exposed to Vinyl Chloride Monomer.

138. NDN 122-0003-0641-0: On the Acute Hepatotoxicity of Inhaled Vinyl Chloride.

139. NDN 122-0001-1439-9: Vinyl Chloride-Induced Angiosarcoma and Hepato-Cellular Carcinoma of the Liver.

CITATIONS

1. **Exposures to polyvinyl chloride, methyl ketone and other chemicals: The pulmonary and non-pulmonary effect. - 93-07 2968285**

Oleru, U. G.; Onyekwere, C.

JOURNAL NAME- INT. ARCH. OCCUP. ENVIRON. HEALTH. vol. 63, no. 7, pp. 503-507 1992 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Community Health, Coll. Med., Univ. Lagos, P. M. B. 12003, Lagos, Nigeria LANGUAGE- English

As part of the continuing assessment of the health impact of exposures in the emerging industries of Nigeria, a study was conducted to determine the relative impact of exposures encountered in four operations of a shoe factory. The health impact assessment consisted of spirometric lung function evaluation and environmental measurement for polyvinyl chloride (1.6 ppm). The study showed that there were differences among exposure subgroups with respect to pulmonary, neurological and dermal toxicities and that these differences were dictated by the types of exposure encountered. Pulmonary toxicity was most severe in the vinyl chloride-exposed subgroup. Neurological impact was most severe in the leather and methylethyl ketone-exposed subgroup and dermal toxicity most severe in the subgroup exposed to plasticizers and stabilizers. There existed substantial deficits in lung function (forced expiratory volume, forced vital capacity FEV sub(1), FVC) among the subgroups relative to normal, non-industrially exposed Nigerians of similar age and height.

2. **Contrasting effects of 1,1,1-trichloroethane on (super(14)C)vinyl chloride metabolism and activation in hepatic microsomes from phenobarbital- and isoniazid-treated rats. - 93-07 2964781**

Baker, M. T.; Ronnenberg, W. C.,Jr.

JOURNAL NAME- TOXICOL. APPL. PHARMACOL. vol. 119, no. 1, pp. 17-22 1993 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial ISSN-0041-008X AUTHOR AFFILIATION- Dep. Anesth., Univ. Iowa, Iowa City, IA 52242, USA LANGUAGE- English

The interaction of 1,1,1-trichloroethane (TCE), a widely used chlorocarbon solvent, on the metabolism and activation of (super(14)C)vinyl chloride in rat hepatic microsomes was investigated to determine the effects of combined exposures to these compounds. In microsomes from phenobarbital (PB)-treated rats, TCE increased vinyl chloride-protein binding and vinyl chloride aqueous metabolite formation over twofold when vinyl chloride 0.32% (v/v) and TCE (0.65%) are incubated together. In contrast, under similar incubation conditions, TCE inhibited vinyl chloride metabolism and protein binding up to 45% in microsomes from isoniazid-treated animals. TCE also inhibited vinyl chloride metabolism and binding in microsomes from untreated rats, but to lesser degree.

3. **Toxicity of polyvinylchloride plastizoles of C, M, P brands for manufacturing medical products. - 93-06 2949555**

Bardov, V. G.; Stepanenko, G. A.; Izotova, P. V.; Shmuter, G. M.; Davydenko, L. M.; Blasiuk, M. G.; Pogorelova, V. I.; Khalavchuk, I. V.

JOURNAL NAME- MED. PROFESS. no. 5, pp. 84-86 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial LANGUAGE- Russian

It is concluded that polyvinyl plastizoles of the mentioned brands should not be used for manufacturing medical products. Only the P brand may be employed for manufacturing balloons for measurement of the blood pressure and for inhalers.

4. **Mortality and cancer incidence among PVC-processing workers in Sweden. - 93-05 2911836**

Lundberg, I.; Gustavsson, A.; Holmberg, B.; Molina, G.; Westerholm, P.

JOURNAL NAME- AM. J. IND. MED. vol. 23, no. 2, pp. 313-319 1993 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Occup. Health, Karolinska Hosp., S-171 84 Stockholm, Sweden LANGUAGE- English

The mortality pattern and the cancer incidence were investigated among 717 men who had been employed for at least 3 months during 1964-1974 in three Swedish PVC-processing plants. The mortality was followed 1964-1986 and the cancer incidence 1964-1984. Expected figures were calculated from Swedish national rates. Among Swedish citizens, the observed mortality and cancer incidence was close to the expected in most diagnoses. Among immigrants, mostly from Finland, there was a marked excess of circulatory deaths. This finding was probably due to the higher incidence of coronary mortality in Finland compared to Sweden. In the whole cohort, five cases of malignant melanoma had occurred as compared to 1.5 expected. This may be due to chance but merits further investigation since an increased incidence of malignant melanoma has previously been found among Norwegian PVC-manufacturing workers.

5. **Migration of vinyl chloride into PVC-bottled drinking-water assessed by gas chromatography-mass spectrometry. - 93-03 2883818**

Benfenati, E.; Natangelo, M.; Davoli, E.; Fanelli, R.

JOURNAL NAME- FOOD CHEM. TOXICOL. vol. 29, no. 2, pp. 131-134 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Lab. Environ. Pharmacol. and Toxicol., Inst. Ric. Farmacol. "Mario Negri", Via Eritrea 62, 20157 Milan, Italy LANGUAGE- English

The migration of vinyl chloride (VC) into drinking-water bottled in polyvinyl chloride (PVC) was studied in relation to storage time, using a gas chromatographic--mass spectrometric method. Trideuterated vinyl chloride was used as internal standard. VC concentrations in the water rose progressively in direct (linear) relation to the time after bottling (about 1 ng/litre/day). The time of storage of PVC-packaged foodstuffs may affect the daily oral intake of this monomer, which in some cases may exceed 100 ng/person/day.

6. **An industry-wide epidemiologic study of vinyl chloride workers 1942-1982. - 93-03 2871077**

Wong, O.; Whorton, M. D.; Foliart, D. E.; Ragland, D.

JOURNAL NAME- AM. J. IND. MED. vol. 20, no. 3, pp. 317-334 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Appl. Health Sci., 181 Second Ave., Suite 628, P. O. Box 2078, San Mateo, CA 94401, USA LANGUAGE- English

The cohort consisted of 10,173 men who had worked for at least one year in jobs involving exposure to vinyl chloride prior to 1 January 1973. These men were employed at 37 plants in the U. S., belonging to 17 companies. Observation of the mortality experience of the cohort was updated from 31 December 1972 to 31 December 1982 (the study now covering 1942-1982). A total of 1,536 cohort members were identified as having died. The observed mortality, by cause, was compared with the expected based on U. S. mortality rates, standaridized for age, race, and calendar time. Analyses by length of exposure, latency, age at first exposure, calendar year of first exposure, and type of products were performed. The study confirmed that the vinyl chloride workers experience of significant mortality excesses in angiosarcoma (15 deaths), cancer of the liver and biliary tract (SMR = 641), and cancer of the brain and other central nervous system (SMR = 180). In addition, the study also found a significant mortality excess in emphysema/chronic obstructive pulmonary disease (COPD) (SMR = 179). On the other hand, the study did not find any excess in either respiratory cancer or lymphatic and hematopoietic cancer. This study also found an increase in biliary tract cancers.

7. **Pulmonary effects of polyvinyl chloride dust exposure on compounding workers. - 93-01 2840822**

Ng, Tze Pin; Lee, Hock Siang; Low, Yong Meng; Phoon, Wai Hoong; Ng, Yuen Ling

JOURNAL NAME- SCAND. J. WORK ENVIRON. HEALTH. vol. 17, no. 1, pp. 53-59 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Community, Occup. and Family Med., Natl. Univ. Singapore, Lower Kent Ridge, 0511 Singapore LANGUAGE- English

Pulmonary effects of Spirometry, chest radiography, environmental measurements, and a questionnaire on respiratory symptoms were used to evaluate the effects of exposure to polyvinyl chloride (PVC) dust on 171 Chinese and Malay PVC compounding workers in comparison with an unexposed reference group. Workers with high cumulative PVC dust exposure had a lower forced expiratory volume in 1 s and forced vital capacity, and a higher prevalence of radiological profusion of small opacities. Wheezing or chest tightness was also significantly more frequent in this group. Unlike previous studies, the PVC compounding workers in this study were exposed to only negligible amounts, if any, of vinyl chloride monomer or thermal degradation products of PVC such as hydrogen chloride, phosgene, or chlorine. The conclusion was drawn that a low grade of pneumoconiosis and a small degree of lung function impairment is associated with PVC dust exposure. Reversible airways obstruction is also likely and warrants further investigation.

8. **A collaborative study of cancer incidence and mortality among vinyl chloride workers. - 92-10 2800898**

Simonato, L.; L'Abbe, K. A.; Andersen, A.; Belli, S.; Comba, P.; Engholm, G.; Ferro, G.; Hagmar, L.; Saracci, R.; et al.

JOURNAL NAME- SCAND. J. WORK ENVIRON. HEALTH. vol. 17, no. 3, pp. 159-169 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Unit Anal. Epidemiol., Int. Agency Res. Cancer, 150 Cours Albert-Thomas, F-69372 Lyon Cedex 08, France LANGUAGE- English

A large European multicentric cohort study has been coordinated by the International Agency for Research on Cancer with the objectives of investigating the dose-response relationship between liver cancer and exposure to vinyl chloride and assessing cancer risk for sites other than the liver. A nearly threefold increase in liver cancer was detected on the basis of 24 observed deaths and 8.4 expected (standardized mortality ratio 286, 95% confidence interval 186-425). The excess from liver cancer was clearly related to time since first exposure, duration of employment, and estimated ranked and quantitative exposures. Other cancer sites investigated on the basis of a priori hypotheses were either not in excess (lung) or apparently unrelated to the exposure variables (brain and lymphoma).

9. **Liver and biliary tract cancer among chemical workers. - 92-09 2774363**

Bond, G. G.; McLaren, E. A.; Sabel, F. L.; Bodner, K. M.; Lipps, T. E.; Cook, R. R.

JOURNAL NAME- AM. J. IND. MED. vol. 18, no. 1, pp. 19-24 1990 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Epidemiol., Health and Environ. Sci., Dow Chem. Co., 1803 Build., Midland, MI 48674, USA LANGUAGE- English

A recent cohort mortality study of male, hourly wage employees of a large Michigan chemical production and research facility had found a greater than expected number of deaths coded to liver and biliary tract cancer. In response, an additional investigation was then undertaken to the 44 liver and biliary tract cancer deaths observed between 1940 and 1982. A random sample of subjects was selected from the total cohort to serve as referents. Company work history records were used to classify cases and referents by work area assignment and potential for exposure to 11 selected chemical agents which have been shown to produce cancer of the liver or biliary passages in experimental animals. Statistically significant associations in both positive and negative directions were found for several work areas within the facility. A suggestive association was found for vinyl chloride monomer, based on five cases with presumed exposure.

10. **Mortality and cancer morbidity in workers exposed to low levels of vinyl chloride monomer at a polyvinyl chloride processing plant. - 92-09 2772927**

Hagmar, L.; Aakesson, B.; Nielsen, J.; Andersson, C.; Linden, K.; Attewell, R.; Moeller, T.

JOURNAL NAME- AM. J. IND. MED. vol. 17, no. 5, pp. 553-565 1990 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Occup. Med., University Hosp., S-221 85 Lund, Sweden LANGUAGE- English

To study whether exposure to low levels of vinyl chloride monomer (VCM) causes increased risk for cancer morbidity and death from ischemic heart disease, a cohort study was performed among 2,031 male workers at a polyvinyl chloride (PVC) processing plant who had been employed for at least 3 months during the period 1945-1980. An almost significantly increased total mortality was found. Deaths caused by violence or intoxication were significantly increased, but not deaths from ischemic heart disease. A significant increase in total cancer morbidity was observed. Respiratory cancers were significantly increased. Furthermore, six brain tumors (vs. 2.6 expected) were observed. This increase, however, was not significant. No liver hemangiosarcoma was observed.

11. **Etheno adducts formed in DNA of vinyl chloride-exposed rats are highly persistent in liver. - 92-08 2749514**

Swenberg, J. A.; Fedtke, N.; Ciroussel, F.; Barbin, A.; Bartsch, H.

JOURNAL NAME- CARCINOGENESIS. vol. 13, no. 4, pp. 727-729 1992 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Univ. North Carolina, Chapel Hill, NC 27599, USA LANGUAGE- English

Preweanling rats were exposed to 600 p.p.m. (4 h/day) of the human carcinogen vinyl chloride for 5 days to determine the molecular dosimetry of DNA adducts in liver, lung and kidney. 7-(2'-Oxoethyl)guanine (7OEG) was the major DNA adduct detected, representing similar to 98% of all adducts. N super(2),3-Ethenoguanine (epsilon G) and 3,N super(4)-etheno-2'-deoxycytidine (epsilon dC) were present at similar to 1% of the 7OEG concentration, while 1,N super(6)-etheno-2'-deoxyadenosine was present in even lower concentrations. Liver had 3- to 8-fold higher amounts of the DNA adducts than lung and kideny. The persistence of all four adducts was determined at 3, 7 and 14 days post-exposure. Whereas 7OEG had a t sub(1/2) of similar to 62 h, all three etheno adducts were highly persistent. After accounting for dilution due to growth-related cell proliferation, epsilon G had a t sub(1/2) of similar to 30 days, while epsilon dC and epsilon dA were not repaired. These data suggest that these cyclic adducts are poorly recognized by liver DNA repair enzymes and have the potential for accumulation upon chronic exposure.

12. **Exposure to vinyl chloride monomer: Results of a cohort study after a seven year follow up. - 92-08 2747367**

Laplanche, A.; Clavel-Chapelon, F.; Contassot, J.-C.; Lanouziere, C.

JOURNAL NAME- BR. J. IND. MED. vol. 49, no. 2, pp. 134-137 1992 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Biostat. Epidemiol., Inst. Gustave Roussy, Rue Camille Desmoulins, 94805 Villejuif Cedex, France LANGUAGE- English

In 1980 a prospective cohort study of exposed and non-exposed subjects was initiated in France by the Institut National de la Sante et de la Recherche Medicale (INSERM U287) in collaboration with occupational physicians from the companies involved. The aim was to evaluate the association between mortality and cancer morbidity and occupational exposure to vinyl chloride monomer (VCM). A total of 1100 subjects exposed to VCM and 1100 nonexposed controls matched for age (to two years), plant, and physician were followed up for seven years (8299 and 8202 person years for exposed subjects and controls respectively) for vital status and health and occupational state.

13. **The persistence of sister-chromatid exchange frequencies in men occupationally exposed to vinyl chloride monomer. - 92-07 2728918**

Fucic, A.; Garaj-Vrhovac, V.; Dimitrovic, B.; Skara, M.

JOURNAL NAME- MUTAT. RES. vol. 281, no. 2, pp. 129-132 1992 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Med. Res. and Occup. Health, Univ. Zagreb, Ksaverska c. 2, Zagreb, Croatia, Yugoslavia LANGUAGE- English

The persistence of sister-chromatid exchange frequencies in a population occupationally exposed to the well known chemical mutagen vinyl chloride monomer was studied. It was shown that increased values of sister-chromatid exchange frequencies were still present in the lymphocytes of workers who had not been exposed for 8-120 days and retired persons for 5-10 years after exposure. The possible ability of vinyl chloride monomer alkylating metabolites to cause long-lasting damage of the DNA molecule is discussed.

14. **Activation of Ki-ras gene by point mutation in human liver angiosarcoma associated with vinyl chloride exposure. - 92-05 2690991**

Marion, M.-J.; Froment, O.; Trepo, C.

JOURNAL NAME- MOL. CARCINOG. vol. 4, no. 6, pp. 450-454 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Hepatitis Res., Inst. Natl. Sante et Rech. Med., Unite 271, 151 Cours Albert Thomas, 69424 Lyon Cedex 03, France LANGUAGE- English

Point mutations of c-ras genes were investigated in human angiosarcomas of the liver associated with occupational exposure to vinyl chloride. DNA prepared from either frozen or paraffin-embedded tissues was amplified by the polymerase chain reaction, and putative point mutations at codons 12, 13, and 61 of c-Ha-ras, c-Ki-ras, and N-ras were analyzed by dot-blot hybridization with allele-specific oligonucleotides. A G multiplied by C arrow right A multiplied by T transition in the second nucleotide at codon 13 of the c-Ki-ras-2 gene was detected in 5 of 6 tumors. This mutation is likely a consequence of vinyl chloride-DNA adduct formation. It leads to the substitution of glycine by aspartic acid in the resulting p21 protein, a consistent amino acid substitution found so far in all types of human cancer exhibiting a codon 13-mutated Ki-ras gene.

15. **Lifetime (149-week) oral carcinogenicity study of vinyl chloride in rats. - 92-03 2660209**

Til, H. P.; Feron, V. J.; Immel, H. R.

JOURNAL NAME- FOOD CHEM. TOXICOL. vol. 29, no. 10, pp. 713-718 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- TNO Toxicol. and Nutr. Inst., P. O. Box 360, 3700 AJ Zeist, Netherlands LANGUAGE- English

A lifetime (149-wk) oral carcinogenicity study of vinyl chloride monomer (VCM) was carried out. Four groups of Wistar rats were used, each consisting of 100 males and 100 females, except for the high-dose group, which comprised 50 males and 50 females. VCM was administered by incorporating polyvinyl chloride powder with a high content of VCM into the diet. The actual exposure levels of VCM were 0 (control), 0.014, 0.13 and 1.3 mg VCM/kg body weight/day. Detailed histopathological examination was restricted to the liver. In the final stage of the study, the mortality in the high-dose group was slightly higher than in controls. A variety of VCM-related liver lesions was found in the high-dose group. The lesions included increased incidences of liver-cell polymorphism, hepatic cysts, foci of cellular alteration, neoplastic nodules, hepatocellular carcinomas and angiosarcomas. Compared with controls, there were increased incidences of hepatic foci of cellular alteration in females of the mid-dose group and of basophilic foci of hepatocellular alteration in females of both the low- and mid-dose groups.

16. **Pathobiochemical response of tracheobronchial lymph nodes following intratracheal instillation of polyvinylchloride dust in rats. - 91-11 2588565**

Agarwal, D. K.; Dogra, R. K. S.; Shanker, R.

JOURNAL NAME- ARCH. TOXICOL. vol. 65, no. 6, pp. 510-517 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Ind. Toxicol. Res. Cent., Post Box 80, M. G. Marg, Lucknow-226 001, India LANGUAGE- English

PVC dust, following a single intratracheal instillation (25 mg/rat), was substantially cleared through the lymphatic circulation and progressively accumulated in the tracheobronchial lymph nodes (TBLN) in a time-dependent manner for up to 1 year. The tissue response in TBLN during 60-270 days post-instillation of PVC dust was characterized by progressive increase in total organ fresh weight, dry weight, DNA, RNA and protein contents, concurrent with the proliferation of macrophages and hyperplasia of reticular cells. Active phagocytosis and enhanced hydrolytic activity in TBLN was evident around 270 days post-instillation by the appearance of PVC-laden macrophages near and within the dust foci, and increased

activity of acid phosphatase, DNAse, RNAse and beta -glucuronidase.

17. **Vinyl chloride-induced DNA adducts. II: Formation and persistence of 7-(2'-oxoethyl)guanine and N super(2),3-ethenoguanine in rat tissue DNA. - 91-10 2555478**

Fedtke, N.; Boucheron, J. A.; Walker, V. E.; Swenberg, J. A.

JOURNAL NAME- CARCINOGENESIS. vol. 11, no. 8, pp. 1287-1292 1990 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Pathol., Campus Box 7095, Univ. North Carolina, Chapel Hill, NC 27599, USA LANGUAGE- English

The formation and persistence of the DNA adducts 7-(2'-oxoethyl)guanine (OEG) and N super(2),3-ethenoguanine (EG) were investigated in preweanling Sprague-Dawley rats exposed to vinyl chloride (VC). The concentrations of OEG and EG were measured in liver, lung, kidney, brain and spleen. HPLC with fluorescence detection was used for OEG detection, and gas chromatography-negative ion chemical ionization mass spectrometry was used for EG detection. In view of the slow loss of EG and its high efficiency for causing base-pair mismatch, the results suggest that EG may be an important DNA adduct in VC-induced carcinogenesis.

18. **Sister chromatid exchanges, proliferating rate index, and micronuclei in biomonitoring of internal exposure to vinyl chloride monomer in plastic industry workers. - 91-07 2510890**

Sinues, B.; Sanz, A.; Bernal, M. L.; Tres, A.; Alcala, A.; Lanuza, J.; Ceballos, C.; Saenz, M. A.

JOURNAL NAME- TOXICOL. APPL. PHARMACOL. vol. 108, no. 1, pp. 37-45 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Pharmacol., Med. Sch., Univ. Zaragoza, Zaragoza, Spain LANGUAGE- English

The frequency of micronuclei (MN), sister chromatid exchange (SCEs), and the proliferating rate index in peripheral blood lymphocytes from 93 individuals were measured. Fifty-two of the individuals were workers in the plastics industry where they were exposed to vinyl chloride monomer while the remaining 41 individuals served as a control group. In our results, an increase of SCEs and MN, as well as inhibited cell kinetics, was observed in the group of exposed workers. Of the tests used, SCE was found to be the most sensitive endpoint for indicating a biological response. However, since methods for restricting the MN analysis to only cells at risk (i.e., second generation interphase cells) were not used, this statement requires verification.

19. **Mutagenicity of vinyl chloride in man: Comparison of chromosome aberrations with micronucleus and sister-chromatid exchange frequencies. - 91-07 2497586**

Fucic, A.; Horvat, D.; Dimitrovic, B.

JOURNAL NAME- MUTAT. RES. vol. 242, no. 4, pp. 265-270 1990 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Med. Res. and Occup. Health, Mose Pijade 158, Zagreb, Yugoslavia LANGUAGE- English

The mutagenic effects on vinyl chloride monomer in man were studied in the lymphocyte culture with 3 methods: the chromosome aberration assay, the micronucleus assay and the sister-chromatid exchange method. Compared with control, values obtained by these tests are increased in workers occupationally exposed to vinyl chloride. In relation to non-smokers, smokers exposed to vinyl chloride show significant increases in sister-chromatid exchange frequencies. The problem of correlating the results of the chromosome aberration assay with micronucleus and sister-chromatid exchange frequencies is discussed.

20. **Tissue reaction to intraperitoneal polymer implants: Species difference and effects of corticoid and doxorubicin. - 91-06 2491947**

Christenson, L.; Aebischer, P.; McMillan, P.; Galletti, P. M.

JOURNAL NAME- J. BIOMED. MATER. RES. vol. 23, no. 7, pp. 705-718 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Artif. Organ Lab., Brown Univ., Providence, RI 02912, USA LANGUAGE- English

The reaction to polyvinyl chloride acrylic copolymer capsules implanted in the peritoneal cavity of rats and mice was studied. Some animals received a slow release dexamethasone pellet, others were pretreated with doxorubicin, in an attempt to minimize the tissue reaction. The tissue reaction was significantly thicker in rats than in mice at both 2 and 6 weeks after implantation. In rats, corticoids decreased significantly the thickness of the reactive layer as compared to control at all time points studied, but doxorubicin had no effect. The tissue reaction in mice was not significantly affected by corticoid treatment. In both species the thickness of the tissue reaction did not increase significantly between 2 and 6 weeks. At 3 days the tissue reaction consisted of an interrupted single layer of macrophages in mice, whereas in rats the reaction consisted of two or three layers of macrophages and polymorphonuclear cells.

21. **Persistent liver dysfunction among workers at a vinyl chloride monomer polymerization plant. - 91-03 2433426**

Ho, S. F.; Phoon, W. H.; Gan, S. L.; Chan, Y. K.

JOURNAL NAME- J. SOC. OCCUP. MED. vol. 41, no. 1, pp. 10-16 1991 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Ind. Health, Minist. Labour, Singapore, Rep. Singapore LANGUAGE- English

Thirteen workers with persistent abnormalities in one or more liver function tests (LFT) at a vinyl chloride monomer (VCM) polymerization plant were investigated. Twelve workers were found to have VCM-induced liver dysfunction based on circumstantial evidence. They were employed between 1971 and 1982 when the VCM levels ranged from 1 to 21 p.p.m. After 1982 when the environmental VCM levels were controlled to below 1 p.p.m., no cases of VCM-induced liver dysfunction were detected. In most cases, glutamic pyruvic transaminase was the earliest parameters to be raised. The second most common parameter is serum gamma glutamyl transpeptidase. The latent period ranged from 1 to 13 years.

22. **Epithelioid hemangioendothelioma of the liver following contact with vinyl chloride. Recurrence after orthotopic liver transplantation. - 91-03 2413211**

Gelin, M.; Van de Stadt, J.; Rickaert, F.; De Prez, C.; Levarlet, M.; Adler, M.; Lambilliotte, J. P.

JOURNAL NAME- J. HEPATOL. vol. 8, no. 1, pp. 99-106 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Dig. Surg. and Gastroenterol., Hop. Erasme, 808 Route Lennik, B-1070 Bruxelles, Belgium LANGUAGE- English

Malignant epithelioid hemangioendothelioma of the liver is a recently recognized and uncommon neoplasm of vascular origin. Few cases have been reported and the treatment remains therefore difficult to define. A relationship to oral contraceptive use has been suggested but no other toxic agents have been incriminated. We report here the first case occurring after a close contact with vinyl chloride. Because of wide hepatic destruction and serious portal hypertension with bleeding varices, the patient underwent orthotopic liver transplantation. After a disease-free interval of 20 months, he died from variceal hemorrhage and encephalopathy due to local tumor recurrence with portal thrombosis. Nevertheless, orthotopic liver transplantation remains the only hope of salvage when extensive liver destruction and life-threatening complications are present.

23. **Rapid analysis of dibutyltin compounds and tricresyl phosphate in polyvinyl chloride (PVC) by thin layer chromatography. - 91-01 2371232**

Baba, T.; Sasaki, S.

JOURNAL NAME- J. FOOD HYG. SOC. JAPAN. vol. 30, no. 4, pp. 321-323 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Osaka City Inst. Public Health and Environ. Sci., 8-34, Tojo-cho, Tennoji-ku, Osaka, Japan LANGUAGE- Japanese

A simple and rapid determination method of dibutyltin compounds and tricresyl phosphate (TCP) contained in polyvinyl chloride (PVC) by thin layer chromatography (TLC) was developed. Contents of dibutyltin compounds and TCP in PVC are limited to lower than 50 ppm and 1,000 ppm, respectively, by the Food Sanitation Law of Japan. Test solution for the proposed method was prepared as follows; 0.2 g of PVC sample as dissolved in tetrahydrofuran (THF), and the polymer was precipitated by adding ethanol at 10 times the THF volume. The filtrate was evaporated to dryness, and the residue was taken up in 1 ml of ethanol, and divided into halves. One half was used for the analysis of dibutyltin compounds, and the other for the analysis of TCP, after hydrolysis with potassium hydroxide. Detection limits of this method for dibutyltin dichloride and TCP were 50 ng and 250 ng, respectively.

24. **Cot mattress biodeterioration and SIDS. - 90-11 2353428**

Richardson, B. A.

JOURNAL NAME- LANCET. vol. 335, no. 8690, p. 670 1990 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Penarth Res. Int., P. O. Box 142, St. Peter Port, Guernsey, Channel Islands LANGUAGE- English

50 Mattresses used in forty-five SIDS incidents were examined. All mattresses contained Scopulariopsis brevicaulis, in the area beneath the infant affected by warmth and perspiration. Incubated samples of the infected materials all generated toxic trihydride gases. PVC coverings usually generate stibine (SbH sub(3)) from a fire retardant additive, antimony trioxide, but also phosphine (PH sub(3)) from the phosphate plasticisers that are used when fire resistance is required. Infection by S. brevicaulis) is not readily visible in PVC. The preferential development of this fungus in cot mattresses should be attributed to the presence of nitrogen compounds in the perspiration. The generation of arsine in this way has been recognized for about 100 years. Phospine, arsine, and stibine are exceedingly toxic with threshold limit values of 0 multiplied by 3, 0 multiplied by 5 and 0 multiplied by 1 ppm, respectively.

25. **1,N super(6)-Ethenoadenosine formation, mutagenicity and murine tumor induction as indicators of the generation of an electrophilic epoxide metabolite of the closely related carcinogens ethyl carbamate (urethane) and vinyl carbamate. - 90-09 2293846**

Leithauser, M. T.; Liem, A.; Stewart, B. C.; Miller, E. C.; Miller, J. A.

JOURNAL NAME- CARCINOGENESIS. vol. 11, no. 3, pp. 463-473 1990 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- McArdle Lab. Cancer Res., Med. Sch., Univ. Wisconsin, Madison, WI 53706, USA LANGUAGE- English

Previous studies from this laboratory showed that vinyl carbamate (VC) was much more carcinogenic than ethyl carbamate (EC) and that both carbamates induced the same spectrum of tumors in mice and rats. In the present studies, VC, but not EC, was found to be oxidized by 3-chloroperbenzoic acid to a derivative that reacted with adenosine to form epsilon Ado. Far more of this etheno nucleoside was formed from VC than from EC when these carbamates were metabolized by cofactor-fortified mouse liver microsomes in the presence of adenosine. Sodium diethyldithiocarbamate strongly inhibited these microsomal reactions and the formation of epsilon Ado in the hepatic RNA of mice administered either carbamate. The data from all these studies are consistent with the proposal that VC epoxide is an ultimate electrophilic and carcinogenic metabolite of EC and VC in the mouse.

26. **Nucleophilic selectivity as a determinant of carcinogenic potency (TD sub(50)) in rodents: A comparison of mono- and bi-functional alkylating agents and vinyl chloride metabolites. - 90-05 2224908**

Barbin, A.; Bartsch, H.

JOURNAL NAME- MUTAT. RES. vol. 215, no. 1, pp. 95-106 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Int. Agency Res. Cancer, 150 Cours Albert-Thomas, 69372 Lyon, Cedex 08, France LANGUAGE- English

Using published data, the carcinogenic potency (TD sub(50)) in rodents of a series of monofunctional alkylating agents, bifunctional antitumor drugs and the vinyl chloride (VC) metabolites chloroethylene oxide (CEO) and chloroacetaldehyde (CAA) was compared to their nucleophilic selectivity. A positive correlation between the log of TD sub(50) estimates and the s values for a series of 14, mostly monofunctional, alkylating agents was observed. This linear relationship also included 2 bifunctional chloroethylnitrosoureas, although their carcinogenic potency was compared to their initial 7-/0 super(6)-alkylguanine ratio rather than their s values. In addition, the carcinogenic potency of 2 alkyl sulfates, which is not yet known accurately, may correlate with their nucleophilic selectivity through the same relationship. By contrast, 2 methyl halides and 5 bifunctional antitumor drugs (nitrogen mustards and azyridinyl derivatives) did not follow this linear relationship: at similar nucleophilic selectivity, they were more potent carcinogens than the above 18 alkylating agents; this may hold true for CEO and CAA too, although further carcinogenicity experiments are needed to calculate their precise TD sub(50) values.

27. **Occupational asthma due to unheated polyvinylchloride resin dust. - 90-05 2214792**

Lee, H. S.; Yap, J.; Wang, Y. T.; Lee, C. S.; Tan, K. T.; Poh, S. C.

JOURNAL NAME- BR. J. IND. MED. vol. 46, no. 11, pp. 820-822 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Ind. Health, Minist. Labour, Singapore, Rep. Singapore LANGUAGE- English

Polyvinylchloride (PVC) resins are widely used in industry. Asthma due to the thermal degradation products of PVC are well documented. In this first case of occupational asthma due to unheated PVC resin dust the patient was exposed to PVC resin dust during the mixing of chemicals used for making plastic seals for bottle caps.

28. **Effects of vinyl chloride on liver function of exposed workers, evaluated by measurements of plasma clearance of the super(99m)Tc-N-2,4-dimethylacetanilido-iminodiacetate complex. - 90-04 2196157**

Studniarek, M.; Durski, K.; Liniecki, J.; Brykalski, D.; Poznanska, A.; Gluszcz, M.

JOURNAL NAME- J. APPL. TOXICOL. vol. 9, no. 4, pp. 213-218 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Nucl. Med., Med. Acad., 92-216 Lodz, Czechoslowacka 8/10, Poland LANGUAGE- English

In 77 males exposed occupationally to vinyl chloride (VC), the plasma clearance (Cl) of super(99m)Tc-N(2,4-dimetnylacetanilido) iminodiacetate ("HEPIDA" complex) was determined. The results were juxtaposed with a scaled assessment of liver parenchyma performance based upon clinical examination and a series of biochemical tests. Detection of the diagnosable damage of liver parenchyma by means of the reduced clearance was sensitive (90%) at the reasonable specificity of 74%. Probability of exclusion of liver damage in patients with the clearance above 240 ml/min 1.73/m super(2) amounted to 92%. There was a significant correlation between degree of exposure to VC and the frequency of low clearance values. It appears that the periodic determination of the super(99m)Tc-HEPIDA clearance in workers exposed to VC allows the assessment of incipient liver damage and signals the need for prophylactic measures.

29. Small airways function in workers processing polyvinyl chloride. - 90-03 2175111

Nielsen, J.; Faahraeus, C.; Bensryd, I.; Aakesson, B.; Welinder, H.; Linden, K.; Skerfving, S.

JOURNAL NAME- INT. ARCH. OCCUP. ENVIRON. HEALTH. vol. 61, no. 7, pp. 427-430 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Occup. Med., University Hosp., S-22185 Lund, Sweden LANGUAGE- English

In a polyvinyl chloride (PVC) processing plant, 20 workers employed as machine attendants and calender operators, and thus exposed to PVC thermal degradation products (PTDP) and phthalic acid esters (PAE; up to 2 mg/m super(3)), were studied. The control group was 19 unexposed workers. The exposed subjects had more symptoms from eyes and upper airways than the controls, probably mainly associated with PTDP. Two (10%) exposed workers had mild work-related asthma vs no control; five (25%) vs one (5%) symptoms of unspecific bronchial hyperreactivity. One exposed subject had a significantly raised level of IgG against phthalic anhydride, indicating that sensitization can occur in PVC processing.

30. Central nervous system malformations in relation to two polyvinyl chloride production facilities. - 90-03 2156732

Rosenman, K. D.; Rizzo, J. E.; Conomos, M. G.; Halpin, G. J.

JOURNAL NAME- ARCH. ENVIRON. HEALTH. vol. 44, no. 5, pp. 279-282 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Michigan State Univ., Dep. Med., B338 Clin. Cent., East Lansing, MI 48824, USA LANGUAGE- English

A modified case-control study was conducted for selected birth defects that occurred among residents who lived in areas that surrounded two vinyl chloride polymerization facilities in New Jersey. Odds ratios for central nervous system defects decreased as the distance the mother's residences were located from the facilities increased. Higher odds ratios for central nervous system birth defects were found in the areas around the plant that had higher vinyl chloride emissions. None of the odds ratios, however, were statistically significant. The differences in concentrations of emissions from the different plants may contribute to the discrepancies reported in previous studies wherein the risk of environmental exposure to vinyl chloride was assessed.

31. Comparison of potency of human carcinogens: Vinyl chloride, chloromethylmethyl ether and bis(chloromethyl)ether. - 90-02 2134729

Van Duuren, B. L.

JOURNAL NAME- ENVIRON. RES. vol. 49, no. 2, pp. 143-151 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Lab. Org. Chem. and Carcinog., Inst. Environ. Med., New York Univ. Med. Cent., New York, NY 10016, USA LANGUAGE- English

The alpha -chloroether carcinogen chloromethylmethyl ether (CME) and its impurity bis(chloromethyl)ether (BCME) are direct-acting alkylating agents. vinyl chloride (VC) is an indirect-acting carcinogen but its accepted carcinogenic intermediate, chloroethylene oxide, is also an alpha -chloroether. Both CME-BCME and VC have been in industrial use since about 1950. They were selected for comparison of potency as human carcinogens using numerous epidemiologic reports. There were 115 deaths due to angiosarcoma of the liver among several hundred thousand VC-exposed workers on the basis of reports from 10 countries during 1955 and 1984. Reports from five countries cited a total of 87 respiratory cancer deaths among only 3024 CME-BCME-exposed workers. If a recent court settlement in the United States is taken into account, the number of respiratory cancer deaths due to CME-BCME rises to 117.

32. Update to vinyl chloride mortality study. - 90-01 2110050

Dahar, W. S.; Bond, G. G.; McLaren, E. A.; Sabel, F. L.; Lipps, T. E.; Cook, R. R.

JOURNAL NAME- J. OCCUP. MED. vol. 30, no. 8, pp. 648-649 1988 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dow Chemical Co., Epidemiol. Health and Environ. Sci., 1803 Build., Midland, MI 48674, USA LANGUAGE- English

NO-ABSTRACT

33. **Disposition of acetone, methyl ethyl ketone and cyclohexanone in acute poisoning. - 89-12 2096992**

Sakata, M.; Kikuchi, J.; Haga, M.; Ishiyama, N.; Maeda, T.; Ise, T.; Hikita, N.

JOURNAL NAME- J. TOXICOL.: CLIN. TOXICOL. vol. 27, no. 1-2, pp. 67-77 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Fac. Pharm. Sci., Higashi-Nippon-Gakuen Univ., Tobetsu, Ishikari 061-02, Japan LANGUAGE- English

A case of coma due to the drinking of a liquid cement for polyvinyl chloride resin, containing acetone, methyl ethyl ketone, cyclohexanone and polyvinyl chloride is described. The patient also simultaneously ingested the alcoholic beverage, sake. After gastric lavage, plasma exchanges and direct hemoperfusions, the patient recovered. The concentrations of these chemicals in plasma and urine were analyzed at various time intervals to estimate the clearance. The elimination half lives for acetone and methyl ethyl ketone were 18 hours and 10 hours, respectively. Although cyclohexanone made up the largest component in the solvents, the blood level was extremely low and a large amount of cyclohexanol, a metabolite of cyclohexanone was detected in the blood and urine.

34. **Cohort and case-control analyses of workers exposed to vinyl chloride: An update. - 89-09 2032644**

Wu, Weiai; Steenland, K.; Brown, D.; Wells, V.; Jones, J.; Schulte, P.; Halperin, W.

JOURNAL NAME- J. OCCUP. MED. vol. 31, no. 6, pp. 518-523 1989 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- NIOSH, Industrywide Stud. Branch, Robert A. Taft Lab., Cincinnati, OH 45226-1998, USA LANGUAGE- English

The mortality in a cohort of workers at a vinyl chloride polymerization plant has been updated, extending the period of observation from 1974 to 1986. Workers may have been exposed to vinyl chloride monomer and/or polyvinyl chloride dust, or may have had no exposure to either substance. Seventy-six percent of the work force worked in jobs with potential exposure to vinyl chloride monomer. Among the total cohort, statistically significant excess risks were observed for liver, lung, and brain cancer. For the subcohort of workers exposed to vinyl chloride monomer, the standardized mortality ratio (SMR) for liver cancer was 333. There were no significant excesses of either brain or lung cancer. To investigate dose response, nested case-control studies for liver, brain, and lung cancer were conducted among the total cohort (including the nonexposed).

35. **Immunochemical profiles of workers differing in the degree of occupational exposure to vinyl chloride. - 89-05 1949057**

Bencko, V.; Wagner, V.; Wagnerova, M.; Batora, J.; Hrebacka, J.

JOURNAL NAME- J. HYG. EPIDEMIOL. MICROBIOL. IMMUNOL. vol. 32, no. 4, pp. 375-384 1988 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Postgrad. Sch. Med. and Pharm., Ruska 85, 100 05 Praha 10, Czechoslovakia LANGUAGE- English

The immunobiochemical studies were conducted in 98 production workers engaged in polyvinyl chloride manufacture from ethylene (group A workers) and in vinyl chloride workers from a chemical plant employing classic production technology from acetylene (group B workers). All workers were examined for serum concentration of immunoglobulins IgG, IgA and IgM and acute reactants lysozyme (LYS), transferrin (TRF), ceruloplasmin (CPL), alpha-1-antitrypsin (A1AT), alpha-2-macroglobulin (A2M) and orosomucoid (ORO). Group A worked in conditions meeting the MAC 10 mg VC multiplied by m super(-3) comparing with group B workers had elevated levels of IgG IgA and IgM. Group B workers differed from group A workers by exhibiting significantly elevated levels of A1AT, and CPL.

36. Carcinogenicity of vinyl chloride in Sprague-Dawley rats after prenatal and postnatal exposure. - 89-03 1901413

Maltoni, C.; Cotti, G. EDITOR- Maltoni, C.; Selikoff, I. J.

JOURNAL NAME- ANN. N. Y. ACAD. SCI. vol. 534, pp. 145-159 1988 DOCUMENT TYPE- Book Monograph MONOGRAPH TITLE- LIVING IN A CHEMICAL WORLD: OCCUPATIONAL AND ENVIRONMENTAL SIGNIFICANCE OF INDUSTRIAL CARCINOGENS. BIBLIOGRAPHIC LEVEL- Analytical, Monographic, Serial AUTHOR AFFILIATION- Inst. Oncol. "F. Addarii", Bologna, Italy LITERARY INDICATOR(S)- K CONFERENCE DATE- 6-10 Oct 1985 CONFERENCE TITLE- International Conference on Living in a Chemical World: Occupational and Environmental Significance of Industrial Carcinogens CONFERENCE LOCATION- Bologna (Italy) LANGUAGE- English

Vinyl chloride was administered by inhalation, 7 hours daily, 5 days weekly, at concentrations of 2500 and 0 ppm, to Sprague-Dawley rats. The treatment was started on 13-week-old breeders and male and female offspring (12-day embryos). The breeders and part of the offspring were exposed for 104 weeks; the other part of the offspring was exposed for 15 weeks only. Under the experimental conditions, vinyl chloride caused an exceptionally high incidence of brain neuroblastomas, liver angiosarcomas, and hepatocarcinomas. The age at start and/or length of treatment may affect the onset of these tumors in different ways.

37. Factors of humoral resistance in workers exposed to vinyl chloride with a view to smoking habits. - 89-01 1875276

Wagnerova, M.; Wagner, V.; Znojemska, S.; Hrebacka, J.

JOURNAL NAME- J. HYG. EPIDEMIOL. MICROBIOL. IMMUNOL. vol. 32, no. 3, pp. 265-272 1988 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Immunol. KHS, Dittrichova 17, 120 07 Prague 2, Czechoslovakia LANGUAGE- English

Serum samples were assayed in 110 workers (59 smokers and 51 non-smokers) at a PVC manufacturing factory. Non-smokers had higher levels of immunoglobulins (IgG, IgA, IgM), while in smokers there was an increase in IgM only. Lysozyme levels (LYS) were elevated in all exposed subjects, but there was a decrease in the total protein (TP) content. Alpha-2-macroglobulin (A2M) and orosomucoid (ORO) were elevated in exposed workers. A significant increase was found in ceruloplasmin (CPL), with smokers having higher levels than non-smokers.

38. Human male exposure to vinyl chloride and possible teratogenic and mutagenic risks: A review. - 89-01 1881289

Uzych, L.

JOURNAL NAME- HUM. TOXICOL. vol. 7, no. 6, pp. 517-527 1988 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- 103 Canterbury Dr., Wallingford, PA 19086, USA LANGUAGE- English

Data suggest that the exposure of human males to vinyl chloride in the workplace, and elsewhere, may be associated with various chromosomal aberrations in lymphocytes and sister chromatid exchanges. Paternal exposure to vinyl chloride may be associated with adverse effects on pregnancy and possibly spermatic alterations. This review is intended to examine critically selected, available data concerning paternal exposure to vinyl chloride and possible reproductive related risks.

39. Hepatocarcinogens induce gene mutations in rats in fibroblast-like cells from a subcutaneous granulation tissue. - 88-12 1845479

Maier, P.; Schawalder, H. P.

JOURNAL NAME- CARCINOGENESIS. vol. 9, no. 8, pp. 1363-1368 1988 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Toxicol., Swiss Fed. Inst. Technol., CH-8603 Schwerzenbach, Switzerland LANGUAGE- English

Gene-mutations at the 6-thioguanine locus, in fibroblast like-cells proliferating on the inside of rat subcutaneous air pouches were analysed. Target cells were exposed directly by injection into the air pouch, or systemically by oral or intraperitoneal administration to three hepatocarcinogens aflatoxin B sub(1), 2-acetylaminofluorene (2-AAF) and vinylchloride. Ethylnitrosourea (ENU) was used as a positive control, and 2-aminofluorene to characterize the pharmacokinetic behaviour of 2-AAF. When administered directly, all chemicals except 2-AAF induced a dose-dependent increase

in gene-mutation frequencies. 2-AAF was mutagenic after oral administration. The highest inducible mutation frequencies with the hepatocarcinogens were 8 to 10 times the spontaneous mutation frequency, but only similar to 10% of that found with ENU.

40. Effects of exposure to vinyl chloride. An assessment of the evidence. - 88-09 1789015

Doll, R.

JOURNAL NAME- SCAND. J. WORK ENVIRON. HEALTH. vol. 14, no. 2, pp. 61-78 1988 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Imperial Cancer Res. Fund, Univ. Oxford, Gibson Build., Radcliffe Infirm., Oxford OX2 6HE, UK LANGUAGE- English

This paper reviews the possible effects of vinyl chloride on the mortality of occupationally exposed men and the carcinogenic effects that might be observed in the general population as a result of environmental pollution with vinyl chloride. The data permit two conclusions. First, men occupationally exposed to vinyl chloride have experienced a specific hazard of angiosarcoma of the liver. Second, any other occupational hazards that may have existed have been small. No positive evidence of a hazard of any nonmalignant disease or any type of cancer other than angiosarcoma of the liver has been found except possibly for a small hazard of lung cancer when exposure was heavy.

41. Increasing evidence of the rise of cancer in workers exposed to vinylchloride. - 88-07 1753809

Smulevich, V. B.; Fedotova, I. V.; Filatova, V. S.

JOURNAL NAME- BR. J. IND. MED. vol. 45, no. 2, pp. 93-97 1988 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- All-Union Cancer Res. Cent., AMS USSR, Moscow, USSR LANGUAGE- English

The results of a cancer mortality study among workers employed in the production of vinylchloride and polyvinylchloride between 1939 and 1977 suggest a significant increase in deaths from malignancies of the lymphatic and haemopoietic tissues. Mortality for tumours of the digestive organs, respiratory system, bone and connective tissues, brain, and skin are also greater than in the general population. There were no registered cases of liver angiosarcoma in the study cohort during the follow up period. The risk of cancer was highest among the workers exposed to concentrations of VC of 300 mg/m super(3) and more who had worked at the plant for 15 to 19 years. The relatively high number of leukaemias and lymphomas in the study group and the absence of liver angiosarcomas probably reflects specific carcinogenic action of different doses of vinylchloride.

42. Exposure to vinyl chloride monomer: Report on a cohort study. - 88-05 1717489

Laplanche, A.; Clavel, F.; Contassot, J.-C.; Lanouziere, C.

JOURNAL NAME- BR. J. IND. MED. vol. 44, no. 10, pp. 711-715 1987 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Stat. Med., 39500 Tavaux, France LANGUAGE- English

In 1980 a prospective exposed/non-exposed cohort study was initiated in France by the Institut National de la Sante et de la Recherche Medicale (INSERM U 287) to evaluate the association between mortality and cancer morbidity and occupational exposure to vinyl chloride monomer (VCM). Eighteen (1 multiplied by 6%) and 15 (1 multiplied by 4%) cases of cancer were reported among exposed and non-exposed subjects, respectively (NS). One case of angiosarcoma of the liver occurred among the exposed group; six cases of lung cancer occurred among exposed subjects and two among non-exposed subjects (NS). The percentage of diseases of the circulatory system was higher in the exposed group than in the non-exposed group: this difference was explained mainly by the high incidence of Raynaud's disease. The percentages of diseases of the respiratory system did not differ between the two groups.

43. **Migration of an organo-tin stabilizer from polyvinyl chloride film to food and food simulating liquids. - 88-02 1653730**

Schwope, A. D.; Till, D. E.; Ehntholt, D. J.; Sidman, K. R.; Whelan, R. H.; Schwartz, P. S.; Reid, R. C.

JOURNAL NAME- DTSCH. LEBENSM.-RUNDSCH. vol. 82, no. 9, pp. 277-282 1986 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Arthur D. Little, Inc., Acorn Park, Cambridge, MA 02140, USA LANGUAGE- English

The migration of the organo-tin stabilizer di(n-octyl) tin S,S'-bis (isooctylmercaptoacetate) from polyvinyl chloride (PVC) to foods and food simulating liquids (FSL) was measured. The stabilizer was radiolabeled and blended to an initial concentration of about 1.8 weight percent. The FSL studied were water, 3% acetic acid, 100, 50 and 8% ethanol, corn oil, and n-heptane. The temperature was 49 degree C. Foods included milk, cola, wine, whiskey, margarine, mayonnaise, and cheese. Except for the semisolid foods, migration was continuous with no indication of cessation.

44. **Early detection and signs of hepatoangiosarcoma among vinyl chloride workers. - 87-11 1612257**

Sugita, M.; Masuda, Y.; Tsuchiya, K.

JOURNAL NAME- AM. J. IND. MED. vol. 10, no. 4, pp. 411-417 1986 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Public Health, Sch. Med., Tokai Univ., Boseidai, Isehara-shi, Kanagawa-ken 259-11, Japan LANGUAGE- English

Health examinations of 108 workers exposed to vinyl chloride monomer (VCM) at a Japanese chemical plant were carried out in 1979. Examinations assessed data on age, height, weight, obesity index, sake consumption, VCM exposure concentration, latent period, cumulative exposure, ICG (indocyano green test), serum bilirubin, GOT (glutamic oxaloacetic transaminase), GPT (glutamic pyruvic transaminase), A1-P (alkaline phosphatase), GGT(gamma -glutamyl transpeptidase), ZTT (zinc turbidity test), LDH (lactate dehydrogenase), cholesterol, TTT (thymol turbidity test), A/G (albumin globulin ratio), and thrombocytes. Variation in VCM exposure did not affect tests of pigment excretion from the liver, such as ICG; thrombocytes; and enzyme activity (such as GPT); nor bilirubin or flocculation reaction in serum.

45. **Respiratory effects of work in retail stores: II. Respiratory symptoms. - 87-10 1591794**

Wegman, D. H.; Eisen, E. A.; Smith, T. J.; Greaves, I. A.; Fine, L. J.

JOURNAL NAME- SCAND. J. WORK ENVIRON. HEALTH. vol. 13, no. 3, pp. 209-212 1987 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Sch. Public Health, Univ. California, Los Angeles, CA 90024, USA LANGUAGE- English

This study examined the relationships between the prevalence of respiratory tract symptoms and estimates of environmental exposures in retail food stores, in particular exposures to emissions from the cutting of polyvinyl chloride wrap. When respiratory symptoms were compared with a measure of cumulative exposure, there was evidence that the prevalence of symptoms of episodic airway narrowing was higher for workers who had been exposed directly or indirectly to meat wrapping operations independent of significant association of these symptoms with allergic or asthmatic history. Whether this finding reflects a nonspecific irritant effect or allergic sensitization cannot be determined from these data. No single substance present in the work environment studied has, as, yet, been identified as associated with these effects.

46. **The vinyl chloride-derived nucleoside, N super(2),3-ethenoguanosine, is a highly efficient mutagen in transcription. - 87-08 1555315**

Singer, B.; Spengler, S. J.; Chavez, F.; Kusmierek, J. T.

JOURNAL NAME- CARCINOGENESIS. vol. 8, no. 5, pp. 745-747 1987 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Donner Lab., Lawrence Berkeley Lab., Univ. California, Berkeley, CA 94720, USA LANGUAGE- English

N super(2),3-Ethenoguanine (N super(2),3- epsilon G) was recently identified in the

liver of vinyl chloride-exposed rats. The authors have now synthesized the nucleoside and the 5'-diphosphate which was copolymerized with CDP. The deoxypolynucleotide complement, synthesized by AMV reversed transcriptase contained, in addition to dG, dC and dT. The total pyrimidine content was approximately equivalent to the N super(2),3- epsilon G content of the template. Incorporation of dC is neither lethal nor mutagenic, while dT incorporation represents a mutagenic event, occurring with similar to 10% frequency. N super(2),3- epsilon G multiplied by dT base pairs can have two hydrogen bonds with minimal helical distortion, as is also the case for N super(2),3- epsilon G. C base pairs. N super(2),3- epsilon G is the only derivative formed in vivo by the human carcinogen, vinyl chloride, that can be shown to have a high probability of causing transitions which could initiate malignant transformation.

47. Utilization of 1, N super(6)-etheno-2'-deoxyadenosine 5'-triphosphate during DNA synthesis on natural templates, catalyzed by DNA polymerase I of Escherichia coli). - 87-07 1537947

Revich, G. G.; Beattie, K. L.

JOURNAL NAME- CARCINOGENESIS. vol. 7, no. 9, pp. 1569-1576 1986 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Verna and Marrs McLean Dep. Biochem., Baylor Coll. Med., Houston, TX 77030, USA LANGUAGE- English

To test whether vinyl chloride-induced mutagenesis might involve ambiguous base pairing of 1 N super(6)-etheno-adenine (epsilon A) during DNA synthesis, the authors examined the base pairing potential of epsilon dATP during DNA synthesis catalyzed by Escherichia coli) DNA polymerase I. Despite the fact that the etheno bridge completely blocks normal Watson-Crick pairing of epsilon A with T, we observed that epsilon dATP could substitute for dATP during primer elongation (although inefficiently). In addition, detectable substitution of epsilon dATP for dGTP and dCTP occurred, indicating that epsilon A exhibits ambiguous base pairing properties. The relative ease of epsilon dAMP incorporation (opposite template T, C and G) appeared to vary considerably at different positions along the template.

48. In vitro studies on the metabolism and covalent binding of (super(14)C)1,1-dichloroethylene by mouse liver, kidney and lung. - 87-07 1537899

Okine, L. K.; Gram, T. E.

JOURNAL NAME- BIOCHEM. PHARMACOL. vol. 35, no. 16, pp. 2789-2795 1986 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Natl. Cancer Inst., Natl. Inst. Health, Build. 37, Rm. 5B-22, Bethesda, MD 20892, USA LANGUAGE- English

The metabolism and covalent binding of 1,1-dichloro(1,2- super(14)C)ethylene (DCE) to subcellular fractions of liver, kidney and lung of C57BL/6N mice have been investigated in vitro. Covalent binding was NADPH- and cytochrome P-450-dependent. The microsomal fraction bound more radiolabel than any other subcellular fraction, and the levels of covalent binding in cell fractions correlated well with their cytochrome P-450 content. Covalent binding by mouse liver and lung microsomes also reflected their cytochrome P-450 content. However, although mouse kidney microsomes contained twice as much total cytochrome P-450 as the lung, no detectable covalent binding of DCE-derived radioactivity occurred in kidney. Omission of NADPH, heat inactivation of microsomes, carbon monoxide, addition of SKF-525A, piperonyl butoxide or reduced glutathione (GSH), all inhibited (40-90%) covalent binding of radiolabel to liver and lung microsomes.

49. A scientific basis for the risk assessment of vinyl chloride. - 87-07 1530781

Swaen, G. M. H.; de Hollander, A. E. M.; Kroes, R.; den Engelse, L.; Mulder, G. J.; Verbeek, A. L. M.; Verschuuren, H. G.; Vogel, E. W.; van der Wielen, A. W.

JOURNAL NAME- REGUL. TOXICOL. PHARMACOL. vol. 7, no. 1, pp. 120-127 1987 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Occup. Med., Univ. Limburg, P. O. Box 616, 6200 MD Maastricht, Netherlands LITERARY INDICATOR(S)- O LANGUAGE- English

In July 1984 the Minister of Welfare, Public Health and Culture, representing the Dutch government, sent a request to the Health Council of The Netherlands to advise on the health risks presented by environmental exposure to several carcinogenic substances. One of these substances was vinyl chloride (VC). On the basis of a working document prepared by the National Institute of Public Health and Environmental Hygiene, a committee of the Health Council of The Netherlands prepared

a report concerning a health risk assessment of VC which was published in May 1986. A short review is presented of the available data and the considerations that formed the basis for the risk assessment of the carcinogenicity of VC to humans. The advice was based mainly on human data from epidemiological studies of workers occupationally exposed to VC. The committee concludes that continuous exposure to 0.001 mg/m super(3) VC corresponds to an additional cancer mortality risk of 10 super(-6) per lifetime. The Dutch government considers this additional risk to the general population to be acceptable.

50. **Quantitative histochemistry of benzaldehyde dehydrogenase in hepatocellular carcinomas of vinyl chloride-treated rats. - 87-01 1423511**

Chieco, P.; Normanni, P.; Moslen, M. T.; Maltoni, C.

JOURNAL NAME- J. HISTOCHEM. CYTOCHEM. vol. 34, no. 2, pp. 151-158 1986
DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Chem. Pathol. Lab., Dep. Pathol., Univ. Texas Med. Branch, Galveston, TX 77550, USA LANGUAGE- English

Hepatocarcinogenesis in rats treated with several chemicals is associated with changes in aldehyde dehydrogenase (AlDH) activity, particularly heterogeneous expression of a "tumor specific" phenotype that is very active with aromatic aldehydes, e.g., benzaldehyde (Bz). Objectives of this study were first, to determine if liver cancers in vinyl chloride-treated rats also expressed this AlDH phenotype, and second, to quantitate the NAD- and NADP-dependent AlDH activity for the substrates Bz and acetaldehyde (Ac) in the cancers and surrounding tissue. All five carcinomas had heterogeneous staining of NADP- and NAD-dependent BzDH and AcDH activity, with clusters of very high-activity cells. More neoplastic cells had high BzDH than high AcDH activity. Only BzDH-NADP was localized predominantly to the carcinoma.

51. **Two stages of cancerogenesis induced by implantation of foreign objects. - 88-12 1408199**

Moyzhess, T. G.; Vasilyev, Yu. M.

JOURNAL NAME- BYULL. EXP. BIOL. MED. vol. 101, no. 5, pp. 604-605 1986
DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- All-Union Cancer Res. Cent., Acad. Med. Sci. USSR, Moscow, USSR LANGUAGE- Russian

Replacement of non-perforated polyvinylchloride films 3.5 months after implantation to CBA mice by perforated polyvinylchloride films or by millipore filters with 0.45 mu m pores led to the development of sarcoma at the site of implantation in 37.0 and 21.4% of cases, respectively. The implantation of only perforated films let to the development of sarcoma in 6.9% of cases; the implantation of filters failed to induce tumour growth. The latent period of tumour development can be divided into two stages. The first stage occurs in the presence of non-perforated film; the second stage ensues in the presence of non-cancerogenic films. Complete removal of films 6 months after implantation prevented tumour development. Non-perforated films serve as initiating agents; non-cancerogenic films act as protectors.

52. **Phthalate ester exposure-air levels and health of workers processing polyvinylchloride. - 88-12 1407499**

Nielsen, J.; Aakesson, B.; Skerfving, S.

JOURNAL NAME- AM. IND. HYG. ASSOC. J. vol. 46, no. 11, pp. 643-647 1985
DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Occup. Med., University Hosp., S-221 85 Lund, Sweden LANGUAGE- English

Exposure to phthalic acid esters (PAE: mainly di-(2-ethylhexyl), diisodecyl and butylbenzyl phthalates) of workers in a polyvinyl chloride processing industry ranged from 0.02 to 2 mg/m super(3) in different job categories. The workers excreted slightly but significantly higher levels of PAE metabolites in urine than controls. In 54 workers studied clinically, there were no indications of peripheral nerve or respiratory system effects. Some biochemical tests were abnormal; these should be studied further.

53. **Statistical modeling of animal bioassay data with variable dosing regimens: Example--vinyl chloride. - 86-10 1372933**

Brown, K. G.; Hoel, D. G.

JOURNAL NAME- RISK ANAL. vol. 6, no. 2, pp. 155-166 1986 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Res. Triangle Inst., P. O. Box 12194, Research Triangle Park, NC 27709, USA LANGUAGE- English

The authors consider animal bioassay experiments with variable dosing regimens in which groups of animals are dosed beginning at different ages and for varying durations. Two response models are discussed and applied to data from an experiment on vinyl chloride exposure of F-344 rats, B6C3F1 and Swiss CD-1 mice, and Syrian Golden hamsters. A multistage model is used to estimate the dose effect on the ordered stages of tumor development. The data for all endpoints and species/strains examined consistently indicate a predominant effect on the first stage, suggesting vinyl chloride is primarily a tumor initiator. This is consistent with evidence from two-stage experiments on this chemical. The second response model adjusts for survival nonparametrically. It is used to test for an age difference in susceptibility, to evaluate alternative exposure durations, and to compare the effectiveness of alternative dosing regimens for detecting carcinogenicity.

54. **The value of some cytoenzymochemical investigations of the leukocytes and platelets in estimating the effects of occupational exposure to benzene, vinyl chloride and carbon disulphide. - 86-10 1354880**

Micu, D.; Mihailescu, E.; Vilau, C.; Tarpa, A.; Chircu, V.; Zgoanta, C.

JOURNAL NAME- REV. ROUM. MED., MED. INTERNE. vol. 23, no. 2, pp. 115-120 1985 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial LANGUAGE- English

Cytoenzymochemical investigations were performed on the leukocytes and platelets from 2,782 workers occupationally exposed to benzene, vinyl chloride or carbon disulphide, in view of detecting the eventual occurrence of cytometabolic disorders induced by these chemical substances. The results obtained demonstrate the utility of such tests for an early detection of some metabolic disorders of the endolymphocytic proteins, carbohydrates or lipids, in view of preventing the occurrence of more severe pathologic consequences.

55. **Application of the "filter model" to a risk assessment for vinyl chloride. - 86-07 1246050**

Olson, C. S.; Schaeffer, D. J.

JOURNAL NAME- J. TOXICOL. ENVIRON. HEALTH. vol. 17, no. 1, pp. 1-22 1986 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- CERL (EN), P. O. Box 4005, Champaign, IL 61820, USA LANGUAGE- English

The filter model was used to estimate thresholds for the induction of cancer from many dose-response sets for inhalation and ingestion exposure to vinyl chloride for rat and inhalation exposure for mouse. Estimates for a variety of end-point combinations were log-normally distributed over about 2 decades from about 1 to 100 ppm for inhalation exposure to rat and 0.1 to 30 ppm for mouse. When the data is transformed to "dose" (milligrams per kilogram body weight per day), the estimates for inhalation and ingestion exposure and also for rat and mouse are similar. Estimates for different experiments carried out for different durations of time (single exposure to 1 yr) are comparable. Since the threshold is an intrinsic property of the biological system, the estimate, even from a protocol for short exposure and less than lifetime observation, can be used directly in a risk assessment as the maximum safe dose.

56. **Effect of vinyl chloride on testis in rats. - 86-04 1154044**

Bi, W.-F.; Wang, Y.-S.; Huang, M.-Y.; Meng, D.-S.

JOURNAL NAME- ECOTOXICOL. ENVIRON. SAF. vol. 10, no. 3, pp. 281-289 1985 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Health, China Natl. Cent. Prev. Med., Beijing, People's Rep. China LANGUAGE- English

A total of 300 male adult Wistar rats were used. Animals were divided into four groups: control, vinyl chloride (VC) 10-, 100-, and 3000-ppm exposed groups. After

exposure to VC, the organ and body weight ratio, such as the kidney, liver, spleen, and heart were increased, but those of the testis were decreased in the experimental groups in the sixth month. The weights of testis were decreased and damage of testicular seminiferous tubules were found in rats by histopathological examination. Incidence of damage of testicular seminiferous tubules in the control, 10-, 100-, and 3000-ppm groups were 18.9, 29.7, 36.5, and 56.0%, respectively. There was an obvious dose-response relation between the concentration of VC and the incidence of testis damage, with a correlation coefficient of 0.993.

57. Clinical studies of workers exposed to polyvinylchloride dust. - 86-04 1142788

Soutar, C. A.; Gauld, S.

JOURNAL NAME- THORAX. vol. 38, no. 11, pp. 834-839 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Occup. Med., 8 Roxburgh Place, Edinburgh EH8 9SU, UK LANGUAGE- English

A previous study showed that exposure of workers to polyvinylchloride (PVC) dust was associated with the presence of small rounded opacities in the chest radiograph, and also with a small average reduction of the forced expiratory volume in one second (FEV sub(1)). Studies have now been carried out on selected men to determine the clinical importance of the presence of small rounded opacities and also to identify any clinical or physiological features associated with PVC dust exposure. Among 28 men with small rounded opacities, complaints of persistent bronchial mucous hypersecretion were more common (nine men) than among 29 men of similar age, smoking habits, and dust exposures, and there was a suggestion that the physical sign of late inspiratory crackles was more frequent among men with opacities than the other men. The authors conclude that these findings are consistent with the suggestion that the radiographic abnormalities caused by PVC dust exposure are not associated with important functional effects or clinical illness. Further studies are desirable to examine the eventual outcome of the syndrome.

58. Angiosarcoma of the liver and other occupational diseases in vinyl chloride workers. - 86-02 1111443

Halama, J.; Becker-Stone, S.; Halama, J. M.

JOURNAL NAME- RADIOLOGE. vol. 25, no. 1, pp. 22-29 1985 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Radioonkolog. Klin., Stadtkrankenhaus Offenbach a. M., Starkenburgring 66, D-6050 Offenbach a. M. FRG LITERARY INDICATOR(S)- D LANGUAGE- German

Occupational diseases resulting from exposure to vinyl chloride (VC) include angiosarcoma of the liver and other neoplasms Among workers exposed to VC we have found capillary abnormalities in the extremities, with scleroderma and Raynaud syndrome, acro-osteolysis, neurological and psychiatric diseases and chromosome abnormalities, as well as abnormal liver metabolism and haematological findings.

59. Comparison of the impact of continuous and intermittent exposure to vinyl chloride, including phenobarbital effect. - 86-02 1108418

Jedrychowski, R. A.; Sokal, J. A.; Chmielnicka, J.

JOURNAL NAME- J. HYG. EPIDEMIOL. MICROBIOL. IMMUNOL. vol. 29, no. 2, pp. 111-120 1985 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Occup. Med., Dep. Toxicol. Eval., 90-950 Lodz, P. O. Box 199, Poland LANGUAGE- English

Rats were subjected to 4 h continuous and intermittent exposure to vinyl chloride (VC) at the time-weighted average concentration of 50,000 mg/m super(3). The studies were focussed on: body weight, liver weight, activity of enzymes in the blood serum, activity of glutathione S-transferase in the liver cytoplasmatic and microsomal fraction, content of free non-protein sulfhydryl groups (NPSH) in the liver and urinary excretion of thiodiglycolic acid (TDGA). VC exposure, both continuous and intermittent, resulted in a decrease of body weight, NPSH depletion in the liver and TDGA urinary excretion. PB effects were manifested by the persistent decrease in rats' body weight, increase in the liver weight, increase in the cytoplasmatic activity of glutathione S-transferase in the liver and increase in TDGA urinary excretion. With none of the tested parameters, except TDGA, statistically significant differences between the continuous and intermittant VC exposure at the same time-weighted average concentration of 50,000 mg/m super(3), were found.

60. **Use of serum bile acids in the identification of vinyl chloride hepatotoxicity. - 85-09 0995125**

Liss, G. M.; Greenberg, R. A.; Tamburro, C. H.

JOURNAL NAME- AM. J. MED. vol. 78, no. 1, pp. 68-76 1985 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Spec. Stud. and Serv. Branch, Minist. Labour, 400 University Ave., Toronto, Ont., Canada LANGUAGE- English

Most previous studies proposing serum bile acids as indicators of hepatic function have been performed in hospitalized patients in whom overt symptomatic liver disease was present. The ability of fasting levels of serum bile acids to identify mild, clinically inapparent chemical liver injury in an occupational setting was compared with that of indocyanine green clearance and routine biochemical liver tests in 67 asymptomatic chemical workers in whom liver biopsies had been performed for medical indicatios. Histologically, 15 were found to have chemical liver injury, 27 had nonchemical liver disease, and 25 were normal. Two serum bile acids, cholylglycine and conjugates of cholic acid, were determined by radioimmunoassay, using 466 "normal" males from the same worker cohort as a reference range. The data identify the fasting level of serum bile acids as a clinically usable indicator of early chemical injury in chemically exposed asymptomatic worker populations with liver dysfunction.

61. **Bronchitis in relation to work. - 85-08 0978732**

Seaton, A. EDITOR- Kuppa, K.

JOURNAL NAME- SCAND. J. WORK ENVIRON. HEALTH. vol. 10, no. 6, pp. 471-472 1984 DOCUMENT TYPE- Book Monograph MONOGRAPH TITLE- PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM OF RESEARCH ON WORK-RELATED DISEASES. ESPOO, FINLAND, 4-8 JUNE 1984. BIBLIOGRAPHIC LEVEL- Analytical, Monographic, Serial AUTHOR AFFILIATION- Inst. Occup. Med., 8 Roxburgh Place, Edinburgh EH8 9SU, Scotland, UK LITERARY INDICATOR(S)- K CONFERENCE DATE- 4-8 Jun 1984 CONFERENCE TITLE- International Symposium of Research on Work-Related Diseases CONFERENCE LOCATION- Espoo (Finland) LANGUAGE- English

The term bronchitis means different things to different people. Work-related bronchitis might include acute irritation or allergic syndromes or chronic cough and airway obstruction. The investigation of such episodes varies according to the suspected problem -- acute symptoms are investigated in the individual and followed up if necessary epidemiologically, while chronic disease requires an epidemiologic approach. Examples of investigations on soldering, polyvinyl chloride manufacturing, and coal mining are quoted.

62. **Across-shift changes in the pulmonary function of meat-wrappers and other workers in the retail food industry. - 85-08 0976733**

Eisen, E. A.; Wegman, D. H.; Smith, T. J.

JOURNAL NAME- SCAND. J. WORK ENVIRON. HEALTH. vol. 11, no. 1, pp. 21-26 1985 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Occup. Health Program, Harvard Sch. Public Health, 665 Huntington Ave., Boston, MA 02115, USA LANGUAGE- English

The objective of this study was to evaluate the acute respiratory effects of polyvinyl chloride (PVC) emissions in the retail food industry. In particular, the aim was to improve on previous estimates of effect by controlling for confounding in the analysis. Pulmonary function was measured before, during, and after the end of the workshift in 83 workers in the retail food industry. All acute changes in forced expiratory volume in 1 s were standardized for lung size before the magnitude of the changes were compared between the workers exposed and unexposed to the use of hot wires for cutting plastic film. No association was found between acute drop in pulmonary function and either direct or indirect exposure in the absence of a history of asthma or allergy to inhaled materials. The borderline significance of an interaction term between exposure and asthma/allergy in a regression analysis suggests that workers with a history of asthma or atopy may have an acute response to hot-wire wrapping emissions.

63. **Pulmonary function and respiratory symptoms in polyvinylchloride fabrication workers. - 85-08 0975615**

Baser, M. E.; Tockman, M. S.; Kennedy, T. P.

JOURNAL NAME- AM. REV. RESPIR. DIS. vol. 131, no. 2, pp. 203-208 1985 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Environ. Health Sci., Johns Hopkins Sch. Hyg. and Public Health, 615 N. Wolfe St., Rm. 7032, Baltimore, MD 21205, USA LANGUAGE- English

The authors performed preshift and postshift spirometry and administered a standardized respiratory symptoms questionnaire to 174 white males currently employed in polyvinylchloride fabrication to examine the acute and chronic respiratory effects of work exposure. Although there were no significant differences between the in-plant comparison group and any department with potential exposures, there was evidence for respiratory effects in the combined group of comparison and exposed workers. In the combined group, duration of employment was significantly associated with decrements in adjusted cross-shift ratio of forced expiratory volume in one second to forced vital capacity (FEV sub(1)/FVC), preshift FEV sub(1)/FVC, and prevalence of chronic cough and chronic phlegm. In nonsmokers, the prevalences of chronic wheeze and chest tightness were high. The age-adjusted prevalence of chronic wheeze in nonsmokers was also elevated 3.54-fold when compared with that in a community study in the literature.

64. **Vinylchloride induced hepatic angiosarcoma. - 85-01 0831447**

Louagie, Y. A.; Gianello, P.; Kestens, P. J.; Bonbled, F.; Haot, J. G.

JOURNAL NAME- BR. J. SURG. vol. 71, no. 4, pp. 322-323 1984 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- 20 Ave. d'Huart (bte 3), 1150 Brussels, Belgium LANGUAGE- English

The relationship between vinylchloride exposure and human angiosarcoma of the liver (ASL) received attention in 1973 when a case of this rare tumour was diagnosed at autopsy.

65. **Epidemiological study of the lung function of workers at a factory manufacturing polyvinylchloride. - 85-01 0830808**

Lloyd, M. H.; Gauld, S.; Copland, L.; Soutar, C. A.

JOURNAL NAME- BR. J. IND. MED. vol. 41, no. 3, pp. 328-333 1984 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Occup. Med., Edinburgh EH8 9SU, UK LANGUAGE- English

A preliminary epidemiological study has been carried out to investigate a report that some men working in a factory manufacturing polyvinylchloride (PVC) had abnormally low values of the single breath diffusing capacity for carbon monoxide (T sub(L)CO). The distribution of standardised T sub(L)CO results from all persons examined was symmetrical and did not indicate an unexpectedly high proportion of men with clinically important impairment of T sub(L)CO. The results of a case-control study showed that, having allowed for age, height, weight, and smoking habit, T sub(L)CO was associated with a history of working in the PVC factory before 1975, and slightly associated with working in jobs where exposure to vinlychloride monomers (VCM) was likely to have been highest. The men with low T sub(L)CO also tended to have smoked more heavily than controls. The relative importance of occupational factors and smoking in relation to low T sub(L)CO is not clear, but the results give some support to the hypothesis that work in the PVC factory before 1975 entailed exposure to a substance that caused impairment of lung function in a small number of men.

66. **Two cases of liver angiosarcoma among polyvinyl chloride (PVC) extruders of an Italian factory producing PVC bags and other containers. - 84-02 0813785**

Maltoni, C.; Clini, C.; Vicini, F.; Masina, A.

JOURNAL NAME- AM. J. IND. MED. vol. 5, no. 4, pp. 297-302 1984 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Bologna Inst. Oncol., Viale Ercolani 4/2, 40138 Bologna, Italy LANGUAGE- English

Two cases are reported of liver angiosarcoma occurring among polyvinyl chloride (PVC) extruders from a small Italian factory producing PVC bags and other containers. The possibility that PVC extrusion carries a risk of liver angiosarcoma is important because of the very large number of people working with extruding,

manufacturing and handling PVC, as compared with the number of people working in PVC polymerization and/or VC production. In the past, the level of vinyl chloride (VC) concentration in PVC extrusion workplaces has been thought to be "safe."

67. **Assessment of mutagenic efficiency of two carcinogen-modified nucleosides, 1,N super(6)-ethenodeoxyadenosine and O super(4)-methyldeoxythymidine, using polymerases of varying fidelity. - 84-02 0806954**

Singer, B.; Abbott, L. G.; Spengler, S. J.

JOURNAL NAME- CARCINOGENESIS. vol. 5, no. 9, pp. 1165-1171 1984 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Lab. Chem. Biodyn. and Space Sci. Lab., Berkeley, CA 94720, USA LANGUAGE- English

In this paper, the authors compare the mutational effectiveness of both 1,N super(6)-ethenodeoxyadenoinse (epsilon dA) and O super(4)-methyldeoxythymidine (O super(4)-MedT) using transcription and replication by polymerases of high and low fidelity. They also describe some effects of chloroacetaldehyde treatment of poly d(A-T). Terminal deoxynucleotidyl transferase (TdT) was used to prepared copolymers of dA and epsilon dA. When used as templates for Escherichia coli) DNA polymerase I (Pol I) and compared with poly (dA), normal dTTP incorporation was not significantly affected by the presence of 7% epsilon dA. It is suggested that epsilon dA generally does not prevent dT incorporation but behaves as a bulky lesion which is bypassed. In contrast to the low mutagenic efficiency of epsilon dA, O super(4)-MedT, in copolymers with dA, directed the misincorporation of 1 dG/12 O super(4)-MedT with Pol I and 1 dG/3 O super(4)-MedT with reverse transcriptase. The data are in agreement with the previous reported mutagenicity of O super(4)-MedT in alternating poly d(A-T, m super(4)T).

68. **Preventive measures against occupational hazards in the PVC production industry. - 84-02 0792264**

Tarkowski, S. EDITOR- Jaervisalo, J.; Pfaeffli, P.; Vainio, H.

JOURNAL NAME- PROG. CLIN. BIOL. RES. vol. 141, pp. 177-189 1984 DOCUMENT TYPE- Book Monograph MONOGRAPH TITLE- INDUSTRIAL HAZARDS OF PLASTICS AND SYNTHETIC ELASTOMERS. BIBLIOGRAPHIC LEVEL- Analytical, Monographic, Serial ISBN- 0-8451-0141-2 AUTHOR AFFILIATION- WHO, Reg. Off. Europe, Copenhagen, Denmark LITERARY INDICATOR(S)- K CONFERENCE DATE- 22-27 Nov 1982 CONFERENCE TITLE- International Symposium on Occupational Hazards Related to Plastics and Synthetic Elastomers CONFERENCE LOCATION- Espoo (Finland) LANGUAGE- English

Only recently have experimental studies and clinical observations shown that multiple systemic disorders can be evoked by exposure to VCM. In direct contact, vinyl chloride is a skin irritant. Such contact with the liquid may cause frostbite after evaporation. Severe eye irritation may also occur. Exposure to high concentrations of VCM causes depression of the central nervous system. Symptoms such as nausea and disorders of vision and auditory response were observed after acute exposure to VCM at concentrations from 10,000 ppm to 25,000 ppm.

69. **Occupational hazards in the VC-PVC industry. - 84-02 0792241**

Nicholson, W. J.; Henneberger, P. K.; Seidman, H. EDITOR- Jaervisalo, J.; Pfaeffli, P.; Vainio, H.

JOURNAL NAME- PROG. CLIN. BIOL. RES. vol. 141, pp. 155-175 1984 DOCUMENT TYPE- Book Monograph MONOGRAPH TITLE- INDUSTRIAL HAZARDS OF PLASTICS AND SYNTHETIC ELASTOMERS. BIBLIOGRAPHIC LEVEL- Analytical, Monographic, Serial ISBN- 0-8451-0141-2 AUTHOR AFFILIATION- Environ. Sci. Lab., Mount Sinai, Sch. Med., CUNY, New York, NY 10029, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 22-27 Nov 1982 CONFERENCE TITLE- International Symposium on Occupational Hazards Related to Plastics and Synthetic Elastomers CONFERENCE LOCATION- Espoo (Finland) LANGUAGE- English

Overall, the results of the analysis of 12 studies of VC production and polymerization workers demonstrate an enormously elevated risk of liver malignancies, the possibility of a twofold increased risk of brain and central nervous system tumors and perhaps, also, of malignancies of the lymphatic and hematopoietic system. However, the role of other agents cannot be excluded in the etiology of nonhepatic malignancies. Bronchogenic carcinoma does not appear to be increased from exposures to VC monomer, although a relationship to PVC dust was suggested in one study. These conclusions must be considered in light of limited data on workers followed more than 25 years from onset of exposure.

70. **Trends in cancer mortality among workers in the synthetic polymers industry. - 84-02 0782214**

Nicholson, W. J.; Henneberger, P. K.; Tarr, D. EDITOR- Jaervisalo, J.; Pfaeffli, P.; Vainio, H.

JOURNAL NAME- PROG. CLIN. BIOL. RES. vol. 141, pp. 65-78 1984 DOCUMENT TYPE- Book Monograph MONOGRAPH TITLE- INDUSTRIAL HAZARDS OF PLASTICS AND SYNTHETIC ELASTOMERS. BIBLIOGRAPHIC LEVEL- Analytical, Monographic, Serial ISBN- 0-8451-0141-2 AUTHOR AFFILIATION- Environ. Sci. Lab., Mount Sinai Sch. Med., City Univ. New York, New York, NY 10029, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 22-27 Nov 1982 CONFERENCE TITLE- International Symposium on Occupational Hazards Related to Plastics and Synthetic Elastomers CONFERENCE LOCATION- Espoo (Finland) LANGUAGE- English

A high risk of death from liver HSA has been documented from past exposures to VC. Similar to other carcinogens, the risk of VC-induced liver HSA appears to increase as the second or third power of time from onset of exposure. It is possible to project future mortality using this power relationship, estimates of VC exposure, and observed mortality to 1980. These projections suggest that 200-600 deaths may occur in the United States and 550-2,800 in Western Europe from liver HSA. These projections also suggest that a 1 ppm standard in the VC industry will go far to protecting workers from future malignant disease.

71. **Toxicity of the components of poly(vinylchloride) polymers additives. - 84-02 0782184**

Fishbein, L. EDITOR- Jaervisalo, J.; Pfaeffli, P.; Vainio, H.

JOURNAL NAME- PROG. CLIN. BIOL. RES. vol. 141, pp. 113-135 1984 DOCUMENT TYPE- Book Monograph MONOGRAPH TITLE- INDUSTRIAL HAZARDS OF PLASTICS AND SYNTHETIC ELASTOMERS. BIBLIOGRAPHIC LEVEL- Analytical, Monographic, Serial ISBN- 0-8451-0141-2 AUTHOR AFFILIATION- Dep. Health and Hum. Serv., FDA, Natl. Cent. Toxicol. Res., Jefferson, AR 72079, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 22-27 Nov 1982 CONFERENCE TITLE- International Symposium on Occupational Hazards Related to Plastics and Synthetic Elastomers CONFERENCE LOCATION- Espoo (Finland) LANGUAGE- English

The major objective of this overview is to highlight the toxicological aspects of a number of the major additives used in PVC production and processing, representative of a spectrum of use categories, principally plastiziers, stabilizers, initiators and flame retardants. This admittedly represents but a small fraction of the chemical substances employed within the 14 classes of additives used in synthetic polymers noted earlier in this issue.

72. **The toxicology of monomers of the polyvinyl plastic series. - 84-02 0782108**

Holmberg, B. EDITOR- Jaervisalo, J.; Pfaeffli, P.; Vainio, H.

JOURNAL NAME- PROG. CLIN. BIOL. RES. vol. 141, pp. 99-112 1984 DOCUMENT TYPE- Book Monograph MONOGRAPH TITLE- INDUSTRIAL HAZARDS OF PLASTICS AND SYNTHETIC ELASTOMERS. BIBLIOGRAPHIC LEVEL- Analytical, Monographic, Serial ISBN- 0-8451-0141-2 AUTHOR AFFILIATION- Natl. Board Occup. Saf. and Health, Unit Occup. Toxicol. Res. Dep., S-17184 Solna, Sweden LITERARY INDICATOR(S)- K CONFERENCE DATE- 22-27 Nov 1982 CONFERENCE TITLE- International Symposium on Occupational Hazards Related to Plastics and Synthetic Elastomers CONFERENCE LOCATION- Espoo (Finland) LANGUAGE- English

Among the thermoplastics, the polyvinyl series is of great commercial and technical importance. The series can be divided into three main groups (1979): Polyvinyl chloride (homopolymer). Vinyl chloride copolymers. Polyvinylidene chloride, polyvinyl acetate, polyvinyl alcohol, polyvinyl acetals, polyvinyl ethers. Of these, the homopolymer and the copolymers vinyl chloride/vinylidene chloride are commercially the most important. The monomers used in these two groups are also the most studied in terms of toxicity compared to the other monomers belonging to the series.

73. Assessment of early hepatotoxicity. - 84-01 0754205

Vihko, R.; Vihko, P.; Maentausta, O.; Pakarinen, A.; Janne, O.; Yrjanheikki, E. EDITOR- Aitio, A.; Riihimaki, V.; Vainio, H.

pp. 309-314 1984 DOCUMENT TYPE- Book Monograph MONOGRAPH TITLE- BIOLOGICAL MONITORING AND SURVEILLANCE OF WORKERS EXPOSED TO CHEMICALS. BIBLIOGRAPHIC LEVEL- Analytical, Monographic ISBN- 0-89116-253-4 AUTHOR AFFILIATION- Dep. Clin. Chem., Univ. Oulu, SF-90220 Oulu 22, Finland CONFERENCE DATE- 4-9 Aug 1980 CONFERENCE TITLE- International Course on Biological Monitoring of Exposures to Industrial Chemicals CONFERENCE LOCATION- Espoo (Finland) LANGUAGE- English

The liver plays the major role in the biotransformation and disposition of environmental agents. It is therefore to be expected that if an environmental chemical is harmful to the liver, sensitive indicators may be needed to reveal a possible early hepatotoxicity deriving from such a low-dose exposure. The authors concentrate on the importance of serum bile function, in groups of subjects exposed to one of the following chemicals of their mixtures: atyrene, a number of organic solvents, polyvinyl chloride, and vinyl chloride monomer.

74. A comparative review of the combustion toxicity of polyvinyl chloride. - 84-01 0737120

Hinderer, R. K.

JOURNAL NAME- J. FIRE SCI. vol. 2, no. 1, pp. 82-83 1984 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- B. F. Goodrich Co., Environ. Health Dep., 500 S. Main St., Akron, OH 44318, USA LITERARY INDICATOR(S)- O LANGUAGE- English

NO-ABSTRACT

75. An evaluation of smoke toxicity and toxic hazard of electrical nonmetallic tubing combustion products. - 84-01 0737113

Packham, S. C.; Crawford, M. B.

JOURNAL NAME- J. FIRE SCI. vol. 2, no. 1, pp. 37-59 1984 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Betr Sci., Inc., 996 South 1500 E., Salt Lake City, UT 84105, USA LANGUAGE- English

Small-scale smoke toxicity tests were performed on polyvinylchloride-based electrical nonmetallic tubing (PVC/ENT) using the National Bureau of Standards (NBS) protocol for nonflaming combustion. An LC sub(50) of 28.5 mg/L was determined, placing PVC/ENT smoke in a toxicity category comparable to smoke from wood. Four large-scale tests were conducted in a 21,734-L room (8 x 12 x 8 ft). In tests involving 18 to 30 linear in. of PVC/ENT with and without fuel-contributing heat sources, it was learned that: a) 30 in. of PVC/ENT developed a 3.3-mg/L smoke concentration and an insufficient HCl concentration to cause death or significant symptoms in test animals (rats) and b) in the presence of a relatively small fire (5-lb wood crib), heat and carbon monoxide became life-limiting prior to HCl.

76. Angiosarcoma and hepatocellular carcinoma in vinyl chloride workers. - 84-01 0736471

Evans, D. M. D.; Williams, W. J.; Kung, I. T. M.

JOURNAL NAME- HISTOPATHOLOGY. vol. 7, no. 3, pp. 377-388 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Histol. Dep., Llandough Hosp., Penarth, Glamorgan CF6 1XX, Wales, UK LANGUAGE- Englisn

The livers from five vinyl chloride workers are described. They show angioformative and hepatocellular growth disturbance in varying proportions: angiosarcoma in four cases, liver cell hyperplasia in all, hyperplastic nodules in three cases and hepatocellular carcinoma in two cases. In one case, the transition between hyperplastic nodule and hepatocellular carcinoma is demonstrated. The relationship between these changes and vinyl chloride exposure is discussed, with evidence that they are causally related.

77. **Incidence of cancer among vinyl chloride and polyvinyl chloride workers. - 84-01 0682978**

Heldaas, S. S.; Langard, S. L.; Andersen, A.

JOURNAL NAME- BR. J. IND. MED. vol. 41, no. 1, pp. 25-30 1984 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Res. Cent., Norsk Hydro a s Porsgrunn Fabrikker, 3900 Porsgrunn, Telemark Sentralsjukehus, 3, Norway LANGUAGE- English

The results of a follow up study of the incidence of cancer and the mortality in a cohort of 454 male workers producing vinyl chloride and polyvinyl chloride are presented. The study population was restricted to employees with more than one year's work experience in the study plant between 1950 and 1969 and the cohort was followed up from 1953 to the end of 1979. Twenty three new cases of cancer were observed compared with 20 multiplied by 2 expected; one case of liver angiosarcoma was found. The possibility of a causal relationship between exposure to vinyl chloride and the development of malignant melanomas is discussed.

78. **Toxicity of vinyl chloride and poly(vinyl chloride): A critical review. - 84-01 0849852**

Wagoner, J. K.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 52, pp. 61-66 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- 8310 Carrleigh Parkway, Springfield, VA 22152, USA LITERARY INDICATOR(S)- KO CONFERENCE DATE- 27-29 Apr 1981 CONFERENCE TITLE- 2. Annual Symposium on Environmental Epidemiology CONFERENCE LOCATION- Pittsburgh, PA (USA) LANGUAGE- English

In 1974, vinyl chloride (VC) was first reported in the open scientific literature to induce angiosarcoma of the liver both in humans and in animals. Additional research has now demonstrated the carcinogenicity of VC to other organs and at lower concentrations. The target organs for VC now clearly include the liver, brain and the lung, and probably the lymphohematopoietic system. The evidence for a carcinogenic risk has been extended to jobs associated with poly(vinyl chloride) exposure. Cases of liver angiosarcoma have been reported among individuals employed in PVC fabrication facilities and an epidemiological study has demonstrated a significant association between exposure to PVC dust and the risk of lung cancer mortality. Cases of angiosarcoma of the liver also have been reported among individuals living in near proximity to vinyl chloride-poly(vinyl chloride) plants. An association between PVC dust and pneumoconiosis also has been demonstrated. On the basis of findings, prudent control of PVC dust in the industrial setting is indicated.

79. **Activity of vinyl chloride monomer in the mouse micronucleus assay. - 84-01 0842078**

Richardson, C. R.; Styles, J. A.; Bennett, I. P.

JOURNAL NAME- MUTAT. RES. vol. 124, no. 2, pp. 139-142 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Imperial Chem. Ind. PLC, Central Toxicol. Lab., Alderley Edge, Cheshire, UK LANGUAGE- English

Vinyl chloride monomer (VCM) has been shown to cause chromosomal damage in peripheral blood lymphocytes taken from people exposed to high levels of the gas and its has been used as a gaseous positive control rat bone marrow clastogen in several studies in this laboratory. The micronucleus (MN) test is a widely accepted rapid test for the detection of cytogenetic damage to use in place of conventional chromosomal analysis. The purpose of this study was to assess the utility of VCM as a suitable gaseous positive control clastogen in the MN test and compare the sensitivity of C sub(57)Bl/6J mice of both sexes to VCM.

80. **Tissue reaction to the intrapleural injection of polyvinyl chloride powder, alpha -quartz and titanium dioxide. - 84-01 0824194**

Grasso, P.; Mason, P. L.; Cameron, W. M.; Sharratt, M.

JOURNAL NAME- ANN. OCCUP. HYG. vol. 27, no. 4, pp. 415-425 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Group Occup. Health Cent., British Petroleum Co. PLC, Chertsey Rd., Sunbury-on-Thames, Middlesex TW16 7LN, UK LANGUAGE- English

A comparative study was conducted to assess the potency of three "dusts" - PVC, alpha -quartz and titanium dioxide - in producing fibrosis at the site of deposition when administered to rats by the intrapleural and intraperitoneal routes. PVC and TiO sub(2) produced little reaction; this consisted mainly of macrophage accumulation with very little fibrosis which reached a peak one week after treatment and showed no evidence of further progress. On the other hand, alpha -quartz produced a severe reaction which consisted principally of fibrous tissue. The reaction was progressive and showed no sign of coming to rest by the end of the study.

81. **Evidence of chloroethylene oxide being the reactive metabolite of vinyl chloride towards DNA: Comparative studies with 2,2'-dichlorodiethylether. - 84-01 0623117**

Gwinner, L. M.; Laib, R. J.; Filser, J. G.; Bolt, H. M.

JOURNAL NAME- CARCINOGENESIS. vol. 4, no. 11, pp. 1483-1486 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Arbeitsphysiol., Univ. Dortmund, Ardeystrasse 67, D-4600 Dortmund 1, FRG LANGUAGE- English

The roles of chloroethylene oxide (CEO) and chloroacetaldehyde (CAA) in carcinogenicity of vinyl chloride (VC) have been studied by comparing biological effects of VC exposure with those of 2,2'-dichlorodiethylether (bis(chloroethyl)ether, BCEE) as a metabolic precursor of CAA. Biological endpoints investigated were covalent protein binding, nucleic acid (RNA and DNA) alkylation and the potency of the two chemical to induce preneoplastic ATPase-deficient foci in rat. From the investigations it is concluded that CEO (which is not formed during metabolism of BCEE and CE), not CAA, is the ultimate carcinogenic principle in VC carcinogenicity.

82. **Sensitive flame-photometric-detector analysis of thiodiglycolic acid in urine as a biological monitor of vinyl chloride. - 84-01 0602018**

Chen, Z. Y.; Gu, X. R.; Cui, M. Z.; Zhu, X. X.

JOURNAL NAME- INT. ARCH. OCCUP. ENVIRON. HEALTH. vol. 52, no. 3, pp. 281-284 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Ind. Hyg. & Occup. Dis. Peking, 100020 Peking, People's Rep. China LANGUAGE- English

A simple and selective method to detect thiodiglycolic acid in urine by flame-photometric-detector of gas chromatograph is described. The detection limit of this method is less than 1 ng without disturbances. Urine from 64 subjects exposed to different air concentration of vinyl chloride from 0.3 ppm to more than 100 ppm in three groups and 78 subjects was detected in this way. A comparison of the results of these groups shows significant differences between the control and two exposed groups.

83. **Evaluation of the pulmonary toxicity of plasticized polyvinyl chloride thermal decomposition products in guinea pigs by repeated CO sub(2) challenges. - 83-02 0577128**

Wong, K. I.; Stock, M. F.; Alarie, Y. C.

JOURNAL NAME- TOXICOL. APPL. PHARMACOL. vol. 3, no. 4, pp. 236-248 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Toxicol. Lab., Dep. Ind. Environ. Health Sci., Grad. Sch. Public Health, Univ. Pittsburgh, Pittsburgh, PA 15261, USA LANGUAGE- English

Male guinea pigs were exposed to thermal decomposition products of plasticized polyvinyl chloride (PVC-A) at different concentrations up to to levels inducing acute lethality. Several groups exposed at sublethal levels were then evaluated for pulmonary performance for a period of 57 days following exposure. Pulmonary performance was evaluated by challenging each animal with a mixture containing 10% CO sub(2), 20% O2d2, and 70% N sub(2). In control animals, this mixtured induced an increase in both tidal volume and respiratory frequency. This hyperventilatory response was greatly depressed during the first 3 day following frequency. This hyperventilatory response was greatly depressed during the first 3 days following exposure and gradually returned to normal during the following weeks with the exception of the highest exposure group which still showed a diminished response 57 days after exposure. The pulmonary toxicity induced by thermal decomposition products of PVC-A is probably related to the very large amount of HCl released during thermal decomposition. The CO sub(2) response test, a nonintrusive and noninvasive method to evaluate pulmonary performance in guinea pigs, is easily performed and appears to be a very promising type of pulmonary function test for

toxicological evaluations.

84. **Neoplastic effect of vinyl chloride in mouse lung. Lower doses and short-term exposure. - 83-02 0576576**

Suzuki, Y.

JOURNAL NAME- ENVIRON. RES. vol. 32, no. 1, pp. 91-103 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Environ. Sci. Lab., Dep. Community Med. & Dep. Pathol., Mount Sinai Sch. Med. City Univ. New York, One Gustave Levy Place, New York, NY 10029, USA LANGUAGE- English

Neoplastic pulmonary effects of lower doses of vinyl chloride and short-term exposure (4 weeks) by inhalation have been studied by light and electron microscopy in 220 mice. Except for dead or seriously sick animals, a large majority of the animals were sacrificed at three different stages: immediately after exposure, 12 weeks later, and 40 or 41 weeks after exposure. Six mice were kept longer than 41 weeks to examine the effects of the chemical after a long-term recovery period. Alveologenic tumors were first observed 10 weeks after exposure to 600 ppm. In the subgroups exposed to higher concentrations the incidence of tumors was higher and their appearance was earlier than in the subgroups exposed to lower concentrations. The findings indicated a dose-response relationship for incidence of alveologenic tumors, and the latency period was inversely related to dose.

85. **Vinyl chloride disease -- Neurological disturbances. - 83-02 0576053**

Langauer-Lewowicka, H.; Kurzbauer, H.; Byczkowska, Z.; Wocka-Marek, T.

JOURNAL NAME- INT. ARCH. OCCUP. ENVIRON. HEALTH. vol. 52, no. 2, pp. 151-157 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Occup. Med. Mining and Metallurgical Ind., ul. Bieruta 12, PL-41-200 Sosnowiec, Poland CONFERENCE DATE- 1979 CONFERENCE TITLE- 3. Industrial and Environmental Neurology Congress CONFERENCE LOCATION- Praha, (Czechoslovakia) LANGUAGE- English

In a plant producing vinyl chloride by the emulsion method 200 workers who were exposed to vinyl chloride for 1 to 25 yr, 58 were free of coplaints and nervous disturbances. An astheno-autonomic syndrome was found in 54 and in 88 in combination with positive neurological findings, i.e. pyramidal syndromes, cerebellar distrubances, trigeminal neuropathy and extraphyramidal symptoms, in various combinations - pyramidal + cerebellar in 12, trigeminal + pyramidal in 7, trigeminal + cerebellar in 5. Headaches, nervousness, decrease in physical strength, loss of memory, sleeping disturbances and somnolence were the most frequent complaints.

86. **Lack of dominant lethal effects in male CD-1 mice after short-term and long-term exposures to vinyl chloride monomer. - 83-02 0553598**

Himeno, S.; Okuda, H.; Suzuki, T.

JOURNAL NAME- TOXICOL. LETT. vol. 16, no. 1-2, pp. 47-53 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Hum. Ecol., Sch. Health Sci., Fac. Med., Univ. Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113, Japan LANGUAGE- English

Dominant lethal studies were conducted with vinyl chloride monomer (VCM) in male CD-1 mice, using short-term (10,000 ppm, 4 h/day, for 5 days) and long-term (5000 ppm, 4 h/day, 5 day/week, for 10 weeks) exposures. There was no evidence of dominant lethal effects due to VCM in either case. Semen examination of male mice after long-term exposure failed to reveal any alteration in sperm motility and shape. Sporadic appearance of giant cells was observed in the tests of males exposed to VCM, but was not considered to affect spermatogenesis.

87. **Evaluation of the association between birth defects and exposure to ambient vinyl chloride. - 83-02 0535781**

Theriault, G.; Iturra, H.; Gingras, S.

JOURNAL NAME- TERATOLOGY. vol. 27, no. 3, pp. 359-370 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Occup. Health & Saf., McGill Univ., 1130 Pine Ave. West, Montreal, Que. H3A 1A3, Canada LANGUAGE- English

Birth defects incidence for infants born to residents of Shawinigan, Canada in 1966-1979 were significantly higher than in three comparison communities. Since there has been a vinyl chloride polymerization plant in this town since 1943 from which ten cases of angiosarcoma of the liver have been identified, this study explores the possible association between exposure to vinyl chloride monomer (VCM) in ambient air and the occurrence of birth defects in the community. The excess of birth defects fluctuated seasonally in a way that corresponded to changes in VCM concentration in the environment. Some descriptive data from this study raised the hypothesis of an association between VCM in the air and birth defects in the exposed community, but as a whole, within the sample size available, such an association could not be substantiated.

88. **Biochemical assessment of the bioreactivity of intratracheally administered polyvinyl chloride dust in rat lung. - 83-01 0508818**

Agarwal, D. K.

JOURNAL NAME- CHEM.-BIOL. INTERACTIONS. vol. 44, no. 1-2, pp. 195-201 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Mater. Sci. Toxicol. Lab., Univ. Tennessee, Cent. Health Sci., 26, South Dunlap, Memphis, TN 38163, USA LANGUAGE- English

The present communication reports a periodic biochemical assessment of the biological reactivity of intratracheally administered PVC in rat lung, over a period of one year. The macromolecular constituents, activity of some soluble enzymes and the rate of lipid peroxidation were measured in lung to investigate the posibility of a structural alteration and/or tissue injury by PVC dust, during the period of an active tissue reaction and beyond. The activity of some mitochondrial enzymes was analyzed as an index of the pulmonary tissue reaction with the polymer, at a time when maximum enhancement of the mitochondrial activity and tisue reaction with PVC dust were demonstrated earlier.

89. **Mitochondrial changes in hepatocytes of rats chronically exposed to vinyl chloride and ethanol. - 83-01 0423260**

Miller, M. L.; Radike, M. J.; Andringa, A.; Bingham, E.

JOURNAL NAME- ENVIRON. RES. vol. 29, no. 2, pp. 272-279 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Univ. Cincinnati Med. Cent., Inst. Environ. Health, 3223 Eden Ave., Cincinnati, OH 45267, USA LANGUAGE- English

Chronic exposure of male rats to 600 ppm vinyl chloride (VC) or VC and 5% ethanol (EtOH) in drinking water induced ultrastructural changes in the mitochondria of hepatocytes. After 6 months of VC/EtOH treatment, hepatocyte mitochondria often contained rigid tubular parallel cristae and dilated cristae with dense inclusions: ethanol ingestion alone did not induce these morphological changes. In animals receiving VC alone, large floccular densities in the mitochondrial matrix were seen occasionally after 6 months of VC inhalation. The numbers and severity of changes in mitochondria increased with duration of exposure and age. The greatest responses observed in mitochondria occurred with the combined treatment of VC/EtOH.

90. **Occupational and environmental damage to the liver. - 83-01 0423204**

Moerl, M.

JOURNAL NAME- MUNCH. MED. WOCHENSCHR. vol. 125, no. 3, pp. 40-44 1983 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Gastroenterol. Abt. an Stoffwechselklinik LVA Wuerttemberg, Bismarckstr. 31, D-6990 Bad Mergentheim, FRG LANGUAGE- German

Year after year, hundreds of new chemicals are being put on the market. Their number doubles every 7 to 8 years. The introduction of a new chemical will never be completely free from one kind of risk or another. The problems involved are discussed taking occupational poisonings (carbon tetrachloride, arsenic and vinyl chloride), and food poisoning (aflatoxins, edible oil) as examples.

91. Cause-specific mortality study on VCM workers. - 83-01 0423107

Ebihara, I.

JOURNAL NAME- J. SCI. LABOU. vol. 58, no. 8, pp. 383-389 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Div. Work Environ. and Occup. Dis., Inst. Sci. Labour, Tokyo, Japan LITERARY INDICATOR(S)- 0 LANGUAGE- Japanese

Cause-specific mortality study on VCM workers employed in M-company was carried out. The cohrt was set up by 226 workmen on 1960 and observed until 1979. No cause of death were statistically significant with p<0.05. However, death from all cause, all cancer, gastric cancer, liver and bilialy tract cancer, lung cancer, leukemia, hypertension, other heart disease, liver cirrhosis, and accident were higher than expected. Death from all cause, all cancer, liver and bilialy tract cancer and lung cancer were not significantly higher with p<0.05 level, however, these causes were significantly higher than Japanese male with p<0.10 level. Moreover, the relative death rates of both liver and bilialy tract cancer and lung cancer were increased in accordance with the length of VCM exposure. The results revealed the possibility of carcinogenic effect of VCM on these sites.

92. Roles of 2-haloethylene oxides and 2-haloacetaldehydes derived from vinyl bromide and vinyl chloride in irreversible binding to protein and DNA. - 83-01 0417777

Guengerich, F. P.; Mason, P. S.; Stott, W. T.; Fox, T. R.; Watanabe, P. G.

JOURNAL NAME- CANCER RES. vol. 41, no. 11, pp. 4391-4398 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Biochem., Vanderbilt Univ. Sch. Med., Nashville, TN 37232, USA LANGUAGE- English

The metabolism of (1,2- super(14)C)vinyl bromide (VBR) to products irreversibly bound to DNA and protein was examined in rat liver microsomes, reconstituted cytochrome systems, and isolates hepatocytes. In the 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.

93. Investigations on the correlation between vinyl chloride (VCM)-uptake and excretion of its metabolites by 15 VCM-exposed workers: II. Measurements of the urinary excretion of the VCM-metabolite thiodiglycolic acid. - 83-01 0382929

Heger, M.; Mueller, G.; Norpoth, K.

JOURNAL NAME- INT. ARCH. OCCUP. ENVIRON. HEALTH. vol. 50, no. 2, pp. 187-196 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Staublungenforschung Arbeitsmed. Westfaelischen Wihelms-Univ. Muenster, D-4400 Muenster, FRG LANGUAGE- German

Fifteen workers employed in a PVC producing plant were investigated concerning their individual vinyl chloride (VCM) exposure and the urinary excretion of the VCM metabolite thiodiglycolic acid (TdGA). The urine concentrations found were in the range 0.94-20.4 mu g/ml. These could be compared with exposure data calculated from VCM air analyses performed by personal air sampling and corrected with respect to the exposure times of the workers. The amounts of TdGA excreted within 24 h were correlated with the effective VCM body concentrations calculated from the exposure data as mean values for 12h periods. This correlation resembles a function of the Michaelis-Menten type. It could be shown that during short exposure periods of less than 5 min, the metabolite formation in relation to the exposure data was lower than during longer periods of exposure although, as would be expected, there were some fluctuations of the exposure level. Therefore, the VCM body concentrations could not normally reach steady state values.

94. Effects on the liver of chemicals encountered in the workplace. - 83-01 0382762

Pond, S. M.

JOURNAL NAME- WEST. J. MED. vol. 137, no. 6, pp. 506-514 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- North California Occup. Health Cent., Build. 30, 5th Floor, San Francisco Gen. Hosp. Med. Cent., 1001 Potrero Ave., San Francisco, CA 94110, USA LITERARY INDICATOR(S)- 0 SUPPLEMENTARY NOTE(S)- Special Issue on Occupational Medicine. LANGUAGE- English

The liver plays a central role in toxicology. It is the primary organ of detoxification and elimination by metabolism of many chemicals. Many workplace chemicals can affect the liver in animals; fewer have been proved to do so in humans. The diverse hepatic effects observed in humans from occupational exposure to chemicals range from fatty infiltration, acute hepatitis and cholestasis to cirrhosis and angiosarcoma. Three important workplace chemicals, prototypes for the toxicities of many others, are carbon tetrachloride, vinyl chloride and the polychlorinated biphenyls (PCB's). These three are described in some detail to highlight principles of occupational toxicology. Most of the hepatic effects produced by chemicals in the workplace have clinical, laboratory and morphological features common to many other forms of liver disease. Therefore, only an astute physician who takes an occupational history will recognize the association between a patient's workplace and liver disease.

95. Cytogenetic effects of epoxy, phenolformaldehyde and polyvinylchloride resins in man. - 83-01 0363484

Suskov, I. I.; Sazonova, L. A.

JOURNAL NAME- MUTAT. RES. vol. 104, no. 1-3, pp. 137-140 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Gen. Genet., Acad. Sci. U. S. S. R., Moscow 117333, USSR LANGUAGE- English

The cytogenetic analysis of persons occupationally exposed to synthetic resins has revealed a true increase in the average frequency of cells with chromosome aberrations: 5.5% for epoxy resin (146 persons), 6.1% for polyvinylchloride (52 persons), and 5.0% for phenolformaldehyde (31 persons). An incidence of 2.4% was observed in the control (74 persons). The average frequency of aberrant chromosomes per cell for al the synthetic resins differed from the control. The average frequency of chromosome breaks per chromosome did not differ significantly from the control. Acentric fragments (single and paired) was the prevalent type of aberration.

96. Raynaud's Phenomenon Caused by Vinyl Chloride. Raynaud-Phaenomen Durch Vinylchlorid. - 82-02 0343469

Graef, K.

JOURNAL NAME- MUENCH. MED. WOCHEMSCHR. vol. 123, no. 41, pp. 1510 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Fachaerztin Kinderkrankheiten, Bernadottestr. 12, D-6000 Frankfurt-Nordweststadt, FRG LANGUAGE- German

NO-ABSTRACT

97. Plasticizer Migration From Polyvinyl Chloride Film to Solvents and Foods. - 82-02 0339683

Till, D. E.; Reid, R. C.; Schwartz, P. S.; Sidman, K. R.; Valentine, J. R.; Whelan, R. H.

JOURNAL NAME- FOOD CHEM. TOXICOL. vol. 20, no. 1, pp. 95-104 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Arthur D. Little, Inc., Acorn Park, Cambridge, MA 02140, USA LITERARY INDICATOR(S)- 0 LANGUAGE- English

Polyvinyl chloride (PVC) films used for food wraps contain significant concentrations of plasticizers, along with other additives. The rate of migration of these plasticizers of foods and food-simulating solvents is the principal concern of this paper, which reviews prior experimental studies and presents new data for radiolabelled dioctyl adipate. Analytical models are described to correlate many of the data, criteria are presented for identifying the controlling step in the mechanism of transfer of plasticizer from PVC films into food-simulating solvents, and tentative recommendations are offered for the selection of food simulants and for the type of experiment necessary to allow an unambigous interpretation of the data.

98. **The Effect of Repeated Vinyl Chloride Exposure on Rat Hepatic Metabolizing Enzymes. - 82-02 0339662**

Du, J. T.; Tseng, M.; Tamburro, C. H.

JOURNAL NAME- TOXICOL. APPL. PHARMACOL. vol. 62, no. 1, pp. 1-10 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Reg. Cancer Cent., Univ. Louisville Sch. Med., Louisville, KY 40292, USA LANGUAGE- English

Sprague-Dawley rats were exposed to 2.8% vinyl chloride for 2 (70 hr), 4 (140 hr), and 6 (210 hr) weeks to determine the sequential biochemical changes related to the oxidation and detoxification ability of hepatic tissue. Glutathione-S-transferase(s) activity using 1,2-epoxy-(p-nitrophenoxy)propane and p-nitrobenzyl chloride as substrates was elevated 17 to 24, 28, and 35 to 42% after 2, 4, and 6 weeks of exposure, respectively, suggesting enzyme(s) induction. Cytochromes P-450, the major protein involved with vinyl metabolism, was reduced after vinyl chloride exposure, confirming reports of others that vinyl chloride metabolites destroy P-450.

99. **Respiratory Illness Caused by Overheating of Polyvinyl Chloride. - 82-02 0337812**

Froneberg, B.; Johnson, P. L.; Landrigan, P. L.

JOURNAL NAME- BR. J. IND. MED. vol. 39, no. 3, pp. 239-243 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Natl. Inst. Occupat. Safety & Health, Robert A Taft Lab., Cincinnati, OH 45226, USA LANGUAGE- English

On 9 August 1979, 62 (30 multiplied by 8%) of 201 workers and one of 60 management personnel in a polyvinyl chloride (PVC) fabricating plant developed acute upper and lower respiratory irritation, headache, nausea, and fainting. All were taken to hospital; none died. Sixty of the patients were women. Interviews two weeks later with 57 affected and 14 unaffected workers disclosed that illness had followed exposure to fumes from an overheated (362 degree C) PVC extruding machine. Fumes were emitted from 1100 until 1150; cases occurred from 1100 until late afternoon.

100. **Progression of Vinyl Chloride Induced Hepatic Fibrosis to Angiosarcoma of the Liver. - 82-02 0337433**

Jones, D. B.; Smith, P. M.

JOURNAL NAME- BR. J. IND. MED. vol. 39, no. 3, pp. 306-307 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Gastroenterol., Llandough Hosp., Penarth, S. Glamorgan, UK LANGUAGE- English

Two vinyl chloride monomer (VCM) workers, who developed non-cirrhotic portal fibrosis and portal hypertension, died from angiosarcoma of the liver five and ten years later respectively, despite withdrawal from occupational exposure. The authors 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.

101. **Angiographic Study of Digital Arteries in Workers Exposed to Vinyl Chloride. - 82-02 0337387**

Falappa, P.; Magnavita, N.; Bergamaschi, A.; Colavita, N.

JOURNAL NAME- BR. J. IND. MED. vol. 39, no. 2, pp. 169-172 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Ist. Radiol. dell'Univ. Cattolica S Cuore, Rome, Italy LANGUAGE- English

Five patients exposed to vinyl chloride were studied by hand angiography and other non-invasive methods, including photoplethysmography, reography, and thermography. Raymaud's phenomenon was present in all five subjects, while acro-osteolysis affected only one. Organic vascular lesions, such as narrowing, segmentary occlusions of digital arteries and bridge collaterals, were found in angiographic studies.

102. **Polyvinyl Chloride Wire Insulation Decomposition II: Consideration of Long Term Health Effects From Chlorinated Hydrocarbons. - 82-02 0336774**

Wallace, D.; Nelson, N.; Gates, T.

JOURNAL NAME- J. COMBUST. TOXICOL. vol. 9, pp. 105-108 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Public Interest Sci. Consul. Serv., 549 West 123 St. New York, NY 10027, USA LANGUAGE- English

Shortly after health status surveys had been completed on the survivors of the Beverly Hills Supper Club Fire and on the firefighters injured during the New York Telephone Fire, individual members of each group complained of new disorders and triggered new post-survey "ministudies". All women polled showed severe uterine dysfunctions, some resulting in hysterectomies or other hospitalization. The Telephone firefighter cohort showed atypical pattern of age distribution of cancer cases and cancer types, compared with the Fire Department as a whole. Literature on presence of chlorinated hydrocarbons in PVC pyrolysis and combustion smoke and on the health effects of chlorinated hydrocarbons is reviewed.

103. **Review of Epidemiologic Study Results of Vinyl Chloride-Related Compounds. - 82-01 0290088**

Apfeldorf, R.; Infante, P. F.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 221-226 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Off. Carcinogen Indentif. Class., Health Stand. Prog., Occup. Safety Health Admin., U. S. Dep. Labor, Washington, D. C. 20210, USA LITERARY INDICATOR(S)- KO CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Epidemiologic study results addressing the carcinogenicity of six compounds related to vinyl chloride (vinylidene chloride, trichloroethylene, perchloroethylene, carbon tetrachloride, ethylene dibromide and epichlorohydrin) are reviewed. The study results suggest an increased carcinogenic risk among workers exposed to epichlorohydrin and to dry cleaning and degreasing solvents. Although several studies report no significant excess of cancer mortality, an evaluation of the design of these investigations demonstrates that these negative cohort studies consisted of populations of insufficient sample size and latency to permit any meaningful conclusions regarding carcinogenic risk. Therefore, experimental studies must be relied upon to determine whether several of these substances pose a potential carcinogenic risk to humans. Available evidence indicates that all of these substances have demonstrated a carcinogenic response in experimental animals and most are mutagenic in experimental test systems.

104. **Review of Experimental Carcinogenesis by Compounds Related to Vinyl Chloride. - 82-01 0290083**

Chu, K. C.; Milman, H. A.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 211-220 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Natl. Cancer Inst., NIH Bethesda, MD 20205, USA LITERARY INDICATOR(S)- KO CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

The experimental carcinogenesis results on six compounds related to vinyl chloride are reported. Vinylidene chloride, given by inhalation, was carcinogenic in male CD-1 mice, male CD rats, Sprague-Dawley rats and male Swiss mice. Trichloroethylene, given by gavage and inhalation, was carcinogenic in the B6C3F1 mice. When given by gavage, perchloroethylene was carcinogenic in the B6C3F1 mice, and dichloroethane was carcinogenic in Osborne-Mendel rats and B6C3F1 mice. Dibromoethane, given by gavage and inhalation, was carcinogenic in B6C3F1 mice, F344 rats and Osborne-Mendel rats. Finally, epichlorohydrin was carcinogenic in male Sprague-Dawley rats and B6C3F1 mice.

105. **Angiosarcoma of the Liver: A Signal Lesion of Vinyl Chloride Exposure. - 82-01 0280071**

Vianna, N. J.; Brady, J.; Harper, P.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 207-210 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Bur. Environ. Epidemiol., New York State Dep. Health, Tower Bldg., Empire State Health Plaza, Albany, NY 12237, USA LITERARY INDICATOR(S)- KO CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Vinyl chloride (VCM) induced angiosarcoma of the liver (ASL) is a rare vascular tumor which might be associated with a wide range of disease states. The possibility that this tumor might be a signal lesion is supported by mortality studies suggesting that cancers of the digestive, respiratory, neurological and lymphatic systems have occurred more often than expected in VCM workers. There is also evidence that certain non-neoplastic disorders, such as pneumoconiosis and excess fetal deaths, may be associated with this chemical. It has been suggested that a gradual increase in the incidence of ASL might have occurred in recent years. This could be a reflection of the long latency period and/or the increased recognition of this entity. Several cases of ASL have occurred in people living in the vicinity of VCM plants. This raises the possibility that low-level exposure to this chemical over a long period might induce ASL.

106. **Power Considerations in Studies of Reproductive Effects of Vinyl Chloride and Some Structural Analogs. - 82-01 0280043**

Hatch, M.; Kline, J.; Stein, Z.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 195-201 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Div. Epidemiol., Sch. Public Health Sergievsky Cent., Columbia Univ., 630 West 168th St., New York, NY 10032 USA LITERARY INDICATOR(S)- KO CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

The authors review the evidence examining the relation of reproductive function and exposure to vinyl chloride and selected structural analogs. Investigation of these compounds for possible reproductive effects has focused on paternal exposure, a much less well studied route than maternal exposure. Drawing on animal models, the authors discuss what is known about the possible reproductive consequences of exposure to the father as well as to the mother. In evaluating the studies of reproductive outcome in relation to vinyl chloride or analogs, the authors consider what biologic model may have been tested and whether there was statistical power to detect moderate increases in risk. Parameters influencing statistical power are reviewed, and recommended sample sizes are set out which would insure sufficient power, in future studies, to detect adverse effects.

107. **Mutagenicity Studies of Vinyl Chloride. - 82-01 0280024**

Fabricant, J. D.; Legator, M. S.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 189-193 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Prevent. Med. & Commun. Health, Div. Environ. Toxicol., Univ. Texas Med. Br., Galveston, TX 77550, USA LITERARY INDICATOR(S)- KO CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Mutagenicity studies in both man and in test organisms clearly demonstrate positive mutagenic activity of vinyl chloride. In terms of the mutagenicity studies using a variety of in vitro procedures covering both eukaryotes and prokaryotes, positive effects were found. Cytogenetic in vivo studies in animals and in humans indicate not only somatic mutations, but also germinal effects with this chemical.

108. Prenatal Susceptibility to Carcinogenesis by Xenobiotic Substances Including Vinyl Chloride. - 82-01 0290004

Rice, J. M.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 179-188 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Perinatal Carcinogen. Sect., Lab. Comp. Carcinogen., Natl. Cancer Inst., Fort Detrick, Frederick, MD 21701, USA LITERARY INDICATOR(S)- KD CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

The carcinogenicity of vinyl chloride for experimental animals when administered transplacentally is reviewed in comparison with known transplacental carcinogens, including those that, like vinyl chloride, are dependent on enzyme-mediated metabolic conversion to a reactive intermediate in maternal or fetal tissues. Vinyl chloride is converted by mixed-function oxidases to the reactive metabolite chlorooxirane, the carcinogenicity of which is also reviewed. Vinyl chloride is unequivocally a transplacental carcinogen for the rat. No evidence exists, however, to support the hypothesis that exposure of male rats to vinyl chloride or any other carcinogen confers an increased risk of tumor development on their progeny. Many structural analogs of vinyl chloride, i.e., substituted ethylenes, are also carcinogenic for adult animals, and can with confidence likewise be predicted to be effective transplacental carcinogens.

109. Vinyl Chloride: Inhalation Teratology Study in Mice, Rats and Rabbits. - 82-01 0289991

John, J. A.; Smith, F. A.; Schwetz, B. A.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 171-177 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Toxicol. Res. Lab., Health Environ. Sci. USA, Dow Chemical U. S. A., Midland, MI 48640, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

These studies evaluated the effects of inhaled vinyl chloride monomer (VCM) on mouse, rat and rabbit embryonal and fetal development. Groups of pregnant CF-1 mice, Sprague-Dawley rats and New Zealand white rabbits were exposed to 500 ppm VCM for 7 hr daily during the period of major organogenesis. Subsequently, other groups of mice were similarly exposed to 50 ppm VCM, and rats and rabbits were exposed to 2500 ppm. While maternal toxicity was observed, exposure to VCM did not cause significant embryonal or fetal toxicity and was not teratogenic in any of the three species at the concentrations tested. Simultaneous exposure of some of the pregnant animals to VCM by inhalation plus 15% ethanol in the drinking water resulted in toxic effects greater than those associated with exposure to VCM alone in the three species. The fetal effects observed were similar to those reported for these three species following administration of ethanol without VCM exposure.

110. Review of Pulmonary Effects of Poly(Vinyl Chloride) and Vinyl Chloride Exposure. - 82-01 0289975

Lilis, R.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 167-169 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Environ. Sci. Lab., Dep. Commun. Med., Mount Sinai Sch. Med. City Univ. New York, One Gustave Levy Place, New York, NY 10029, USA LITERARY INDICATOR(S)- KD CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

The contributions of several recent reports to the definition of pulmonary effects of PVC dust inhalation are reviewed. Granulomatous reaction, with inclusion of PVC particles in macrophages and histocytes, and associated interstitial pulmonary fibrosis have been found to lead to exertional dyspnoea, diffuse micronodular chest radiographic opacities and restrictive pulmonary dysfunction. The effects of vinyl chloride (VC) monomer (gas) on proteins and the immunologic mechanisms triggered by the altered protein are possible mechanisms for the development in some cases of interstitial pulmonary fibrosis secondary to VC exposure.

111. **Excess Lung Cancer Risk in a Synthetic Chemicals Plant. - 82-01 0289944**

Waxweiler, R. J.; Smith, A. H.; Falk, H.; Tyroler, H. A.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 159-165 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Industry-wide Stud. Br., Div. Surveill., Hazard Eval. Field Stud., Natl. Inst. Occup. Safety Health, 4676 Columbia Parkway, Cincinnati, OH 45226 USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

A standardized mortality ratio of 1.49 for respiratory system cancer (42 observed deaths versus 28.2 expected, $p < 0.01$) was observed among a cohort of 4806 males employed at a synthetic chemicals plant since its startup in 1942. Upon review of pathologic material, the excess was found to be limited to adenocarcinoma and large cell undifferentiated lung cancer. Many of the workers had been exposed to vinyl chloride, as well as to chlorinated solvents, poly(vinyl chloride) (PVC) dust, acrylates and acrylonitrile. To evaluate the association between lung cancer and occupational chemical exposures, detailed work histories for each cohort member were combined with exposure ratings for each of 19 chemicals for each job for each calendar year since 1942. A serially additive expected dose model was then constructed which compared the doses of the chemicals observed for the lung cancer cases to the doses expected based on subcohorts without lung cancer individually matched to the cases. PVC dust appeared to be the most likely etiologic agnet ($p = 0.037$). Time trends of PVC dust exposure indicated a potential latent period of 5-16 years before death.

112. **Epidemiological Study of Pneumoconiosis in the Italian Poly(Vinyl Chloride) Industry. - 82-01 0289760**

Mastrangelo, G.; Saia, B.; Marcer, G.; Piazza, G.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 153-157 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Ist. Med. Lavoro, Univ. Studi Padova, Via Facciolati 71, Padua, Italy LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Among 1216 workers employed in a poly(vinyl chloride) production factory, 20 cases of pneumoconiosis were found. None of these workers had had previous exposure to organic or inorganic dusts; 731 had been exposed to PVC dust (employed in drying, sacking and blending of polymer) and 485 had been exposed to monomer alone. Chest x-ray films were read by two independent physicians utilizing the ILO/UC Pneumoconiosis Classification, 1971. X-ray abnormalities were characterized by limited profusion, irregular type and low gravity; in a small percentage of cases these were associated with slight restrictive respiratory function impairments.

113. **Mortality and Cancer Rates Among Workers in the Swedish PVC Processing Industry. - 82-01 0289740**

Molina, G.; Holmberg, B.; Elofsson, S.; Holmlund, L.; Moosing, R.; Westerholm, P.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 145-151 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Occup. Toxicol. Unit, Dep. Occup. Med. Labor Med. Div., Dep. Occup. Safety, Box 100, 26 Stockholm, Sweden LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Personnel lists from four PVC-processing industries were collected on production of employees with at least three months of employment at the beginning of 1945 and the last day of employment December 31, 1974. Of 2073 persons, 103 could not be followed up, because they had moved abroad. The remaining persons comprise the cohort of 1970 individuals who were analyzed and compared with the national population with respect to mortality from various diseases and cancer morbidity. The death risk from myocardial infarction is elevated in the cohort. The myocardial infarction risk related to vinyl chloride exposure is discussed in relation to earlier studies on the vascular effects of vinyl chloride.

114. Mortality Among PVC-Fabricating Employees. - 82-01 0289722

Chiazze, L.,Jr.; Ference, L. D.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 137-143 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Div. Biostat. Epidemiol., Georgetown Univ. Sch. Med., 3750 Reservoir Road, N. W., Washington, DC 20007, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

The results of a cross-sectional mortality study of 3847 deaths occurring among current and former (white) employees of 17 PVC fabricators during 1964-1973 are presented. Sex-race-cause-specific proportionate mortality ratios (PMR's) were computed by using two separate standards: one, the U. S. mortality in 1968: the second, U. S. mortality for the individual years 1964-1973. In addition, a case-control analysis, based upon 44 breast cancer deaths among white female employees, is presented. PMR's are significantly different from unity for all cancers, and for cancers of the digestive system among both white males and white females. Although observed deaths significantly exceeded expectations for cancer of the breast, a subsequent case-control analysis reveals no statistically significant relative risks for breast cancer.

115. Poly(Vinyl Chloride) Processes and Products. - 82-01 0289705

Wheeler, R. N.,Jr.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 123-128 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Union Carbide Corp., P. O. Box 8361, South Charleston, WV 25303, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Poly(vinyl chloride) resins are produced by four basic processes: suspension, emulsion, bulk and solution polymerization. PVC suspension resins are usually relatively dust-free and ganular with varying degrees of particle porosity. PVC emulsion resins are small particle powders containing very little free monomer. Bulk PVC resins are similar to suspension PVC resins, though the particles tend to be more porous. Solution PVC resins are smaller in particle size than suspension PVC with high porosity particles containing essentially no free monomer. The variety of PVC resin products does not lend itself to broad generalizations concerning health hazards. In studying occupational hazards the particular PVC process and the product must be considered and identified in the study.

116. Effectiveness of Federally Required Medical Laboratory Screening in the Detection of Chemical Liver Injury. - 82-01 0289683

Tamburro, C. H.; Greenberg, R.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 117-122 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Liver Res. Cent., Div. Digest. Dis., Dep. Med., Univ. Louisville Sch. Med., Louisville, KY 40201, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

The increasing concern of industrialized societies over the potential health hazard of synthetic chemicals in the occupational environment has led to government requirements for medical laboratory screening of workers. The specific tests for such screening programs are most often selected on the basis of medical experience which utilized them in symptomatic or hospitalized populations. Required screening tests for hepatic injury including cancer in vinyl chloride workers has been systematically and prospectively studied in an industrial population working with synthetic rubber and plastics.

117. **Epidemiology of Hepatic Angiosarcoma in the United States: 1964-1974. - 82-01 0289886**

Falk, H.; Herbert, J.; Crowley, S.; Ishak, K. G.; Thomas, L. B.; Popper, H.; Caldwell, G. G.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 107-113 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Chronic Dis. Div., Cent. Environ. Health, Cent. Dis. Control, Public Health Serv., U. S. Dept. Health & Hum. Serv., Atlanta, GA 30333, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

A nationwide survey of hepatic angiosarcoma (HAS) in the United States during the years 1964 through 1974 identified 168 cases. Of these, 42 cases (25%) were associated with known etiologic factors, such as vinyl chloride monomer exposure during preparation of poly(vinyl chloride), use of Thorotrast in angiography, exposure to inorganic arsenic, and treatment with androgenicanabolic steroids; 126 cases (75%) are of uncertain etiology. HAS most often affects males (ratio of approximately 3:1), peaks in the sixth and seventh decades of life (somewhat earlier than other sarcomas of the liver) and appears to occur more often in the industrialized Northeast and Midwest (although reporting artifact may be a factor). There is an extraordinary relative risk for poly(vinyl chloride) polymerization workers; there may also be other chemical-industrial associations that require further investigation. Prospective epidemiologic studies of HAS should be considered as a means of identifying other causative factors (e.g., chemicals or drugs) related to HAS.

118. **Epidemiologic Study of Vinyl Chloride Workers: Mortality Through December 31, 1972. - 82-01 0289851**

Cooper, W. C.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 101-106 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- 2150 Shattuck Ave., Suite 401, Berkeley, CA 94704, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

A population of 10,173 men, employed in 37 plants, was identified as having worked for at least one year in jobs involving probable exposure to vinyl chloride monomer (VCM) prior to January 1,1973. Of the 9677 men whose vital status was determined, 707 were known to have died. For 699, death certificates were obtained. The standardized mortality ratio (SMR) for all causes was 89, that for all malignancies was 104. The only type of malignancy found in significant excess was in the category of malignant neoplasms of the brain and other parts of the nervous system.

119. **German Investigations on Morbidity and Mortality of Workers Exposed to Vinyl Chloride. - 82-01 0289847**

Weber, H.; Reinl, W.; Greiser, E.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 95-99 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Staatlicher Gewerbearzt, Duesseldorf, FRG LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Two studies on mortality and morbidity of workers exposed to vinyl chloride monomer (VCM) which have been carried out on behalf of the Ministry of Labour, Health and Social Affairs on Northrhine-Westphalia are reported.

120. **Observations of the Site-Specific Carcinogenicity of Vinyl Chloride to Humans. - 82-01 0289637**

Infante, P. F.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 89-94 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Office Carcinogen Identt. & Class., Health Stand. Prog., Occup. Safety Health Admin., U. S. Dep. Labor, Washington, DC 20210, USA LITERARY INDICATOR(S)- KO CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

A review of epidemiologic studies of workers exposed to vinyl chloride (VC) was conducted. Some of these studies comprised small cohorts and thus were insensitive in the evaluation of carcinogenic response for sites that do not demonstrate a high relative risk. Other larger studies used methodology and design that precluded an interpretation of the results. Such limitations were acknowledged by some authors.

121. **Results of Sputum Cytology Among Workers Exposed to Vinyl Chloride Monomer and to Poly(Vinyl Chloride). - 82-01 0289630**

Maltoni, C.; Lodi, P.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 85-88 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Oncol. Tumor Cent., Bologna, Italy LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

The results of systematic cytological sputum examinations of 3,380 Italian VC-PVC industry workers and of 2,287 workers in other industries at different potential risk and chosen as control groups are reported. The results indicate an increase in cellular abnormalities and dysplasias in the epithelium of the respiratory tract among VC-PVC workers. These data are in line with experimental results showing that VC produces lung tumors in mice and with early epidemiological evidence among exposed workers.

122. **Preliminary Observations of the Effect of Inhalation of PVC in Man and Experimental Animals. - 82-01 0289617**

Wagner, J. C.; Johnson, N. F.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 83-84 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Med. Res. Council, Pneumoconiosis Unit, Llandough Hosp., Penarth, Wales, UK LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Attention has been focussed, both in man and experimental animals, on the effects of inhalation of the gas monomer, vinyl chloride. There are now strict regulations for the control of the monomer gas, but the particles are regarded as nuisance dust and their emission is not covered by specific legislation. These studies on rats, where both inhalation and implantation methods of exposure have been used, and examination of tissue from human cases exposed to paste polymers, indicate that these small particles can only be regarded as evidence of exposure, and on present evidence there is no indication of causation of significant pulmonary disease. Techniques have been developed by which these particles can be demonstrated in ordinary histological preparations and by transmission electron microscopy.

123. **Pneumoconiosis in Animals Exposed to Poly(Vinyl Chloride) Dust. - 82-01 0289801**

Groth, D. H.; Lynch, D. W.; Moorman, W. J.; Stettler, L. E.; Lewis, T. R.; Wagner, W. D.; Kommineni, C.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 73-81 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Div. Biomed. & Behav. Sci., Dep. Health Hum. Serv., Natl. Inst. Occup. Safety Health, Robert A. Taft Lab., Cincinnati, OH 45226, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Rats, guinea pigs and monkeys were exposed by inhalation (6 hr/day, 5 days/week) for up to 22 months to a 13 mg/m super(3) concentration of PVC dust. Autopsies on rats and guinea pigs were performed after 12 months of exposure and on monkeys after 22 months of exposure. Lung function tests were performed on monkeys after 9, 14 and 22 months of exposure. Aggregates of alveolar macrophages containing PVC particles were found in the lungs of all animals. These aggregates were more numerous in the monkey lungs. No fibrosis or significant cellular infiltrates were present in or near these cellular aggregates. No significant effects on pulmonary function could be demonstrated in the monkeys exposed to PVC. Under the conditions of this experiment, inhaled PVC produced a benign pneumoconiosis.

124. **Cancer Induction Following Single and Multiple Exposures to a Constant Amount of Vinyl Chloride Monomer. - 82-01 0289585**

Hehir, R. M.; McNamara, B. P.; McLaughlin, J.,Jr.; Williqan, D. A.; Bierbower, G.; Hardisty, J. F.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 63-72 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- U. S. Consum. Prod. Safety Comm., Westwood Towers Build., Rm. 738, 5401 West Blvd., Washington, D. C. 20207, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Vinyl chloride monomer (VCM), already identified as a human animal carcinogen, was selected as a model agent to explore an area of concern for single and intermittent low level exposure. In traditional cancer bioassay, animals are repeatedly exposed over their lifespan to a dose of suspected chemical. In the current studies rats and mice were exposed in an inhalation chamber to single one-hour doses of VCM ranging from 50 to 50,000 ppm.

125. **Effect of Ethanol on Vinyl Chloride Carcinogenesis. - 82-01 0289572**

Radike, M. J.; Stemmer, K. L.; Bingham, E.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 59-62 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Univ. Cincinnati Med. Cent., Dep. Environ. Health, Kettering Lab., 3223 Eden Ave., Cincinnati, OH 45267, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Four treatment groups (80 male Sprague-Dawley rats/group) were used in a 2 x 2 factorial design: inhalation of 600 ppm vinyl chloride (VC) 4 hr/day, 5 days/week for 1 year; VC and ingestion of 5% ethanol in water (v/v); filtered air and ethanol; filtered air. Ingestion of ethanol was begun 4 weeks prior to inhalation of VC and continued for life or termination of the study at two and one-half years from the first VC exposure. In this model system, ethanol potentiated the carcinogenic response to VC in the liver and produced an excess of neoplasms in animals receiving ethanol alone. Ethanol with or without VC had a strong tumorigenic effect on the endocrine system. These results indicate that ethanol is a cocarcinogen in relation to the carcinogen VC.

126. Effects of Aging on the Induction of Angiosarcoma. - 82-01 0289550

Groth, C. H.; Coate, W. B.; Ulland, B. M.; Hornung, R. W.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 53-57 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Div. Biomed. & Behav. Sci., Natl. Inst. Occup. Safety Health, Robert A. Taft Lab., Cincinati, OH 45226, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Adult, Sprague-Dawley albino rats of four different ages (6, 18, 32 and 52 weeks) were exposed to 940 ppm vinyl chloride by inhalation for 24 weeks, 5 days/week, 7 hr/day. In each age group, there were 110 to 128 males and the same number of females. The similarly housed control group, which was not exposed to vinyl chloride, consisted of the same number of males and females in each age group. All animals that died spontaneously, or were sacrificed moribund, or were killed at scheduled times (3, 6 and 9 months after initial exposure) were autopsied. All organs were examined grossly, and several tissues from each animal were examined microscopically. This study demonstrated that older adult animals and females are more susceptible to the angiosarcoma-inducing effects of vinyl chloride than young adult animals and males, respectively.

127. Neoplastic and Nonneoplastic Effects of Vinyl Chloride in Mouse Lung. - 82-01 0289538

Suzuki, Y.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 31-52 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Environ. Sci. Lab., Dep. Commun. Med. & Dep. Pathol., Mount Sinai Sch. Med. City Univ. New York, One Gustave Levy Place, New York, NY 10029, USA LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

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 months (large doses and long-term exposure). Pulmonary tumors were observed in 26 of 27 experimental animals. The neoplastic effect of vinyl chloride of smaller doses (100, 10, 1 and 0 (control) ppm) and shorter exposure (four weeks) was studied in lungs of 120 mice. A dose-response relation was considered in the incidence of the alveologenic tumor production of vinyl chloride. It is concluded that mouse lung is an extremely sensitive indicator of the oncogenicity of vinyl chloride.

128. Carcinogenicity Bioassays of Vinyl Chloride Monomer: A Model of Risk Assessment on an Experimental Basis. - 82-01 0289531

Maltoni, C.; Lefemine, G.; Ciliberti, A.; Cotti, G.; Carretti, D.

JOURNAL NAME- ENVIRON. HEALTH PERSPECT. vol. 41, pp. 3-29 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. Oncol., Bologna, Italy LITERARY INDICATOR(S)- K CONFERENCE DATE- 20-21 Mar 1980 CONFERENCE TITLE- Conference to Reevaluate the Toxicity of Vinyl Chloride Monomer, Poly(Vinyl Chloride) and Structural Analogs CONFERENCE LOCATION- Bethesda, MD (USA) LANGUAGE- English

Data are presented regarding the final results of the Bentivoglio (Bologna) project on long-term carcinogenicity bioassays of vinyl chloride (VC). The experimental project studied the effects of the monomer, administered by different routes, concentrations and schedules of treatment, to animals (near 7000) of different species, strains, sex and age. This is the largest experimental carcinogenicity study performed on a single compound by a single institution. The results indicate that VC is a multipotential carcinogen, affecting a variety of organs and tissues.

129. **Vinyl Chloride Disorder. - 82-01 0289438**

Walker, A. E.

JOURNAL NAME- BR. J. DERMATOL. vol. 105, no. 21, pp. 19-21 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Royal Hosp., Chesterfield, Derbyshire, UK LITERARY INDICATOR(S)- KO CONFERENCE DATE- 10-11 Apr 1981 CONFERENCE TITLE- Meeting of the British Association of Dermatologists CONFERENCE LOCATION- Stratford-upon-Avon (UK) LANGUAGE- English

The medical hazards associated with exposure to vinyl chloride monomer (VCM) highlight two important aspects of industrial medicine: firstly, the long latent interval which may occur between initial exposure to a toxic substance and the appearance of clinical evidence of damage; and secondly, the important role of animal experimental work in alerting physicians to the potential toxic effects of chemical substances.

130. **Detection of N super(2),3-Ethenoguanine in DNA After Treatment With Chloroacetaldehyde in vitro. - 82-01 0284926**

Oesch, F.; Doerjer, G.

JOURNAL NAME- CARCINOGENESIS. vol. 3, no. 6, pp. 663-665 1982 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Toxicol., Univ. Mainz, Obere Zahlbacher St. 67, D-6500 Mainz, FRG LANGUAGE- English

The reaction of chloroacetaldehyde, a reactive metabolite of the carcinogen vinyl chloride, with DNA produces in addition to the hitherto known adducts, 1,N super(6)-ethenoadenine and 3,N super(4)-ethenocytosine, an ethenoguanine adduct, namely N super(2)-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 h.p.l.c., its mass spectrum and fluorescence spectrum are identical with those published in the literature for the chemically synthesized N super(2),3-ethenoguanine. The formation of only this guanine derivative out of several theoretically possible reaction products allows the formulation of a reaction scheme.

131. **Polyvinyl Chloride Pulmonary Disease. - 82-01 0243551**

Pinsker, K. L.; Fell, S.; Kamholz, S. L.

JOURNAL NAME- CHEST. vol. 80, no. 6, p. 768 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dep. Pulmon. Med., Montefiore Hosp. & Med. Cent., Albert Einstein Coll. Med., Bronx, NY 10467, USA LANGUAGE- English

A 30-year-old fireman presented to Montefiore Hospital and Medical Center in 1977, two years after he was exposed to heavy concentrations of PVC fumes emanating from burning cable insulation.

132. **Power Considerations in Epidemiologic Studies of Vinyl Chloride Workers. - 82-01 0243550**

Beaumont, J. J.; Breslow, N. E.

JOURNAL NAME- AM. J. EPIDEMIOL. vol. 114, no. 5, pp. 725-734 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Industrywide Studies Branch F-8, Natl. Inst. Occup. Safety. Hlth., 4676 Columbia Pkwy., Cincinnati, OH 45226, USA LANGUAGE- English

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.

133. **Follow-Up Study on the Carcinogenicity of Vinyl Chloride and Vinylidene Chloride in Rats and Mice: Tumor Incidence and Mortality Subsequent to Exposure. - 82-01 0229393**

Hong, C. B.; Winston, J. M.; Thornburg, L. P.; Lee, C. C.; Woods, J. S.

JOURNAL NAME- J. TOXICOL. ENVIRON. HEALTH. vol. 7, no. 6, pp. 909-924 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Battelle Seattle Res. Ctr., 4000 N. E. 41st Street, Seattle, WA 98105, USA LANGUAGE- English

Carcinogenic and other toxic effects on rats and mice were examined during a 12-mo period following exposure to vinyl chloride (VC) or vinylidene chloride (VDC). The results suggest that exposure to vinyl halides at dose levels lower than those that elicit a significant increase in cancer incidence during the lifetime of the animal may, nonetheless, increase the risk of early death or moribundity from toxic pre- or subcarcinogenic effects. At dose levels higher than those consistent with the physiological defense or repair capabilities of the cell, ultimate tumor incidence becomes proportionate to length of exposure and may reflect the number of carcinogenic events elicited during the exposure period.

134. **Evidence for Endothelial Cell Origin of Vinyl Chloride-Induced Hepatic Angiosarcoma. - 82-01 0184978**

Fortwengler, H. P.,Jr.; Jones, D.; Espinosa, E.; Tamburro, C. H.

JOURNAL NAME- GASTROENTEROLOGY. vol. 80, no. 6, pp. 1415-1419 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dept. Med., Div. Digestive Diseases Nutr., Dept. Pathol., Univ. Louisville Sch. Med., Louisville, KY, USA LANGUAGE- English

Previous reports of hepatic angiosarcoma have not clearly defined the cellular type from which this tumor arises. 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.

135. **Neurological Changes in Vinyl Chloride-Exposed Workers. - 82-01 0184376**

Styblova, V.; Lambl, V.; Chumcal, O.; Kellerova, V.; Paskova, V.; Vitocovoya, J.; Zlab, L.

JOURNAL NAME- J. HYG. EPIDEMIOL. MICROBIOL. IMMUNOL. vol. 25, no. 3, pp. 233-243 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dept. Neurology, Med. Fac. Hygiene, Charles Univ., Prague LANGUAGE- English

Vinyl chloride (VC) toxicity for the human organism is not still fully clear. Because of a lack of more detailed neurological studies among the VC-exposed persons, we conducted field investigations among the occupationally exposed workers in a plant where there was six years before put into operation a workshop with a considerable VC hazard.

136. **Ultrastructure of Hepatic Angiosarcoma in Rats Induced by Vinyl Chloride. - 82-01 0170812**

Spit, B.; Feron, V. J.; Hendriksen, F. M.

JOURNAL NAME- EXP. MOL. PATHOL. vol. 35, no. 2, pp. 277-284 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Inst. CIVO-Toxicology Nutr. TNO, P. O. Box 360, 3700 AJ Zeist, The Netherlands LANGUAGE- English

The hepatic angiosarcoma studied was from a male Wistar rat having been exposed to vinyl chloride monomer (VCM) by the oral route for 120 weeks. 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 also 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.

137. **Cancer Mortality of a Group of Canadian Workers Exposed to Vinyl Chloride Monomer. - 82-01 0170763**

Theriault, G.; Allard, P.

JOURNAL NAME- J. OCCUP. MED. vol. 23, no. 10, pp. 671-676 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Dept. Social & Preventive Med. Sch. Med., Laval Univ., Ste-Foy, Que., Canada, G1K 7P4 LANGUAGE- English

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 five years 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 in the exposed group. The standardized mortality ratio for digestive cancer was also higher than that of the general population.

138. **On the Acute Hepatotoxicity of Inhaled Vinyl Chloride. - 82-01 0170707**

Tatrai, E.; Ungvary, G.

JOURNAL NAME- ACTA MIORPHOL. ACAD. SCI. HUNG. vol. 29, no. 2-3, pp. 221-226 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Orszagos Munka- es Uezemegeszseguegyi Intezet, H-1450 Budapest, Nagyvarad ter 2., Hungary LANGUAGE- English

Acute toxicity of vinyl chloride exposure was studied by morphological methods in three species (mouse, rat, rabbit). In rats and rabbits exposure to 1500 ppm of vinyl chloride for 24 hours did not cause pathological changes. In mice shorter inhalation (4 and 8 hours) resulted in circulatory changes, while longer exposure (12 and 24 hours) caused vasomotor paralysis followed by characteristic shock; subsequent alterations could be seen in the liver and lungs. The acute hepatotoxicity of vinyl chloride could not be proved.

139. **Vinyl Chloride-Induced Angiosarcoma and Hepato-Cellular Carcinoma of the Liver. - 82-01 0116268**

Koischwitz, D.; Lelbach, W. K.; Lackner, K.; Hermanutz, D.

JOURNAL NAME- FORTSCHR. GEB. RONTGENSTR. NUKLEARMED. vol. 134, no. 3, pp. 283-290 1981 DOCUMENT TYPE- Journal Article BIBLIOGRAPHIC LEVEL- Analytical, Serial AUTHOR AFFILIATION- Radiol. Klinik der Univ. Bonn, Roentgenabteilung Medizinische Klinik 5300 Bonn-Venusberg, FRG LANGUAGE- German

Three patients with industrial exposure to PVC are described, who developed angio-sarcomas of the liver; in one patient this was combined with a multi-locular primary hepato-cellular carcinoma. The epidemiology, clinical features and diagnosis are discussed, with particular reference to angiography, sonography and computerized tomography. The non-invasive methods, such as computerized tomography and sonography, are the techniques of choice if an angio-sarcoma is suspected after long exposure to PVC.

SUBJECT TERM INDEX

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