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# Health Effects of Vinyl Chloride Monomer: An Annotated Literature Collection

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## Introduction

In January 1974, the report of the deaths of four workers in the vinyl chloride-poly(vinyl chloride) (VC-PVC) industry from rare angiosarcoma of the liver triggered one of the most intensive epidemiological and toxicological searches in the history of industrial medicine.

The monomer, vinyl chloride,  $\text{CH}_2 = \text{CHCl}$ , a colorless gas with a faintly sweet and pleasant odor, is presently produced at an annual rate of 5 billion pounds in the United States. First synthesized and investigated in Germany in 1835 by Regnault, VC did not enter the industrial category until World War II, when its polymerization capabilities were recognized and rapidly exploited. The polymer, PVC, a powdery white crystal first produced commercially in the United States in 1939, now forms the basis of a vast plastics industry with an average annual growth rate of 14%, a 1973 production level of over 4 billion pounds, and an employee roster of approximately 350,000 people.

The reactive monomer is suspected as the toxic agent and carcinogen. The point of greatest worker exposure is in the polymerization processes. Hand-cleaning of polymerization reactors was established as a causal factor when acroosteolysis, one of the symptoms of vinyl chloride disease, developed among reactor cleaners in the 1960s. Since that time the industry has sought to improve processes and curb losses of the monomer, but investigations

by the Environmental Protection Agency's (EPA) Task Force confirm that an excess of 200 million pounds of VC and over 50 million pounds of PVC are discharged into the environment each year. A document entitled, "Preliminary Assessment of the Environmental Problems Associated With Vinyl Chloride and Polyvinyl Chloride" by the EPA Task Force is included in the literature compilation.

On October 4, 1974 the Occupational Safety and Health Administration of the Department of Labor published a new Standard for Exposure to Vinyl Chloride which was to take effect January 1, 1975 but was postponed, pending appeal by the Society of Plastics Industry to the Supreme Court. It set an exposure limit of 1 ppm averaged over an 8-hr period with a ceiling of 5 ppm averaged over any period not exceeding 15 min. The Federal Register notice of this Standard includes the background of the problem, and carcinogenicity findings, as well as the scope and feasibility of the standard.

## Literature

The literature on VC has proliferated rapidly as the concern and resources of science, medicine, labor, industry, and government have been mobilized to elucidate mechanisms of VC toxicity as well as real and potential exposure hazards. The scientific community is striving to formulate, in the context of vinyl chloride, an index to the risks inherent in an ever-widening circle of chemicals, industries, processes, and exposed populations.

Two major conferences have been held this past year: the New York Academy of Sciences'

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"Toxicity of Vinyl Chloride-Polyvinyl Chloride" convened on May 10 and 11, 1974 with proceedings in Volume 246 of *Annals of the New York Academy of Sciences* and the National Institute of Environmental Health Sciences' "Public Health Implications of Components of Plastics Manufacture" on July 29-31, 1974 resulting in this Issue of *Environmental Health Perspectives*.

Our compilation of annotated literature references is directed toward the health aspects of vinyl chloride with a few key historical and analytical references included. Annotations were prepared from the published reports except for a few instances in which time did not allow their acquisition or translation; in these cases, the abstract source used is noted with the citation.

Until 1960 literature detailing the toxic effects of vinyl chloride was sparse; more recently, however, the number of published reports has risen sharply. This trend is noted in the selected reports of this compilation: 1835-1959 (125 years), 17 reports; 1960-1969 (10 years), 43 reports; 1970-1974 (5 years), 102 reports.

Major sources of references in the compilation include:

*Abstracts of World Medicine*, 41: (1967)-45: (1974)  
*Air Pollution Abstracts*, 2(5): (1971)-5(6): (1974)  
*Biological Abstracts*, 1: (1926)-58(12): (1974)  
*Chemical Abstracts*, 21: (1927)-81(11): (1974)  
*Chemical Titles*, No. 1-14 (1974)  
*Excerpta Medica, Section 16, Cancer*, 25: and 26: (8) (1974)  
*Current Journals*  
 MEDLINE Data System  
 TOXLINE Data System  
 Oak Ridge National Laboratory Data Systems

The reference collection has been made a part

of the data base holdings of the Oak Ridge National Laboratory's Information Center Complex and will be updated as the literature accumulates.

## Acknowledgments

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## Abstracts

<1>

Allen, T.H., Spacecraft atmospheres. Part II. Contaminants., Environmental Biology, Altman, P.L. and Dittmer, D.S., (Eds.), Fed. Aser. Soc. Exp. Biol., Bethesda, MD Section No. 82: 326 (1966).

During Mercury space flights, microcontaminants were collected by sorption on carbon and later separated and identified. A concentration up to 3 ppm (if dispersed at one time through the cabin volume) of vinyl chloride was collected. Construction materials were the chief source of contamination.

DEGRADATION; DEPOLYMERIZATION

<2>

American Conference of Governmental Industrial Hygienists, Vinyl chloride., Documentation of the Threshold Limit Values. American Conference of Governmental Industrial Hygienists 3rd. ed.: pp.277-278 (1971).

The Threshold Limit Value (TLV) for vinyl chloride (VC) is 200 ppm or approximately 770 mg/m<sup>3</sup>. The gas is flammable with anesthetic properties at concentrations of 8 to 12%. At this level, VC causes cardiac arrhythmias and sensitization in dogs. Lethal concentration is 30-40%. Examinations by Mutchler and Kraser of 97 VC workers between 1950 and 1967 failed to discover any overt condition due to vinyl chloride. Six clinical parameters were altered, however. Alterations in beta lipoprotein, icterus index, and bromosulfalein retention time may have physiologic significance. A time-weighted average of 300 ppm could result in liver dysfunction.

STANDARDS; OCCUPATIONAL EXPOSURE; HUMAN; LIVER; CARDIOVASCULAR; DOG

<3>

Anghelescu, F.; Otolu, M.; Dobrinescu, E.; Magi-Paraschiv-Domsios, L.; Dobrinescu, G.; Ganea, V., Consideratii clinico-patogenice asupra fenomenului Raynaud la muncitorii din industria policlorurii de vinil. (Clinico-Pathogenic considerations on Raynaud's phenomenon in the employees of the polyvinyl chloride industry.), Med. Interna 21: 473-482 (1969).

Eight employees in the vinyl chloride industry exhibited Raynaud's phenomenon in both hands and, in 3 cases, in the toes. Micronodules were present on the back sides of the hands in 3 cases. Acroosteolysis was detected by radiology. Vasomotricity and thermoregulatory disturbances were found, with 6 of the patients sub-febrile. On changing jobs the phenomenon disappeared in 3 of the patients and persisted in attenuated form in the 5 others. Evident improvement was obtained by guanethidine sulfate--an antihypertensive agent.

Rom.; Eng. Summ.

RAYNAUD'S PHENOMENON; ACROOSTEOLYSIS; BONE; SKIN; OCCUPATIONAL EXPOSURE; HUMAN; CARDIOVASCULAR; THERAPY; CASE STUDY

<4>

Anonymous, Vinyl chloride at molecular level., Sci. News 106(5): 71 (1974).

A recent conference emphasizing vinyl chloride monomer was conducted at Pinehurst, NC by the National Institute of Environmental Health Sciences. This timely gathering of research investigators from colleges and universities, plastics and chemical industries, and government agencies interchanged the most recent knowledge about vinyl chloride effects on the human body and the magnitude of the plastics problem.

CONFERENCE; NIEHS

<5>

Anonymous, White fingers., JAMA 215(4): 631 (1971).

A.G. Maurice Raynaud published his treatise on the condition now known as Raynaud's phenomenon in 1862. Intermittent color changes in fingers and toes are elicited by exposure to cold or by emotion, and may be primary or secondary to neurovascular disturbances, organic vascular disease, cold injuries, cold agglutination of erythrocytes or cryoproteineemia, toxins such as arsenic, ergot, nicotine, or lead, or may be of traumatic origin. Both toxins and trauma are implicated in the finding of Raynaud's phenomenon and acroosteolysis in the polyvinyl chloride industry. This editorial lauds the cooperation between industry and the medical profession in meeting their responsibilities to workers in this instance.

RAYNAUD'S PHENOMENON; OCCUPATIONAL EXPOSURE; REVIEW; EPIDEMIOLOGY; ACROOSTEOLYSIS

<6>

Anonymous, Vinyl chloride to get emission standard., Chem. Eng. News 52(38): 6-7 (Sept. 23, 1974).

Although no scientific evidence indicates that vinyl chloride emissions into the atmosphere pose a hazard to people living near the vinyl chloride and polyvinyl chloride resin manufacturing plants, some hazard does exist. EPA estimates that 200 million pounds of vinyl chloride and 50 million pounds of polyvinyl chloride are discharged annually into the environment. Presently available technology could reduce emissions from chloride resin plants by 75%, and from vinyl chloride plants by 90% with a resulting increase in cost of about 4¢ per pound.

STANDARDS; NON-OCCUPATIONAL EXPOSURE

<7>

Anonymous, How hazardous to health is vinyl chloride?, JAMA 228(11): 1355, 1363, 1364 (1974).

Production workers, warehouse workers where vinyl chloride is stored, and workers of fabrication installations using the polymer, all risk liver damage from vinyl chloride. Vinyl chloride disease, in addition to liver damage, can include damaged pulmonary function, thrombocytopenia, enlarged spleen, excessive production of immature erythrocytes, acroosteolysis, and Raynaud's phenomenon in the hands. The usual battery of liver function tests do not reliably detect the periportal fibrosis that precedes sarcoma growth. The liver does not return to normal for 2.5 years after the worker changes jobs and is removed from exposure. Eleven cases of hepatic angiosarcoma have been discovered in retrospective investigations; additionally, one child of an angiosarcoma patient has developed a primary hepatoma. Eighty percent of Goodyear workers examined by the team from Mt. Sinai School of Medicine showed some evidence of pulmonary obstructive disease after 20 years exposure to vinyl chloride fumes. In a biochemical survey of Goodyear workers in Louisville, no significant changes were observed for serum levels of lactic dehydrogenase, alkaline phosphatase, bilirubin, or SGOT. However 66% of the workers, compared with 0.02% of a general hospital population sample, had elevated levels of factor IV of lactic dehydrogenase. An experimental bile acid clearance test raised hopes of a screening test for vinyl chloride hepatic fibrosis. Extensive prospective-retrospective studies of polyvinyl chloride workers have begun.

LIVER; DIAGNOSTIC; HUMAN; OCCUPATIONAL EXPOSURE; BIOCHEMISTRY; LUNG; ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON

<8>

Anonymous, PVC dangers being studied., J. Environ. Health 37(1): 67 (1974).

On February 12, 1974, the National Institute of Occupational Safety and Health (NIOSH) sponsored a briefing for management and labor representatives from the vinyl chloride and polyvinyl chloride

R&S 135400

<8> CONT.

industries. NIOSH presented plans for development of recommended standards, medical surveillance and research programs, industrywide epidemiologic studies, and additional toxicological investigations. B.F. Goodrich Co. reported that they have increased safety activities and research, reduced exposure levels below 50 ppm on a time-weighted average, installed new equipment, developed advanced monitoring systems, and instituted a safety education program for employees. NIOSH in Cincinnati is directing an epidemiological study which is probably the most intense in the 3-year history of the organization.

#### OCCUPATIONAL EXPOSURE; STANDARDS

<9>

Anonymous, Spectrum: News of the month., Environment 15(5): 22(1973).

Liquor in polyvinyl chloride bottles was temporarily banned by the Food and Drug Administration (FDA) because contamination up to 20 ppm vinyl chloride monomer was discovered. FDA is required by law to set tolerances on packaging materials contaminating food and beverages. About 30 American distillers have used the plastic containers for up to 4 years, and must now prove the inadvertent additive harmless.

#### FOOD; HUMAN

<10>

Anonymous, Preliminary economic impact study says VC monitoring to cost \$100,000 per plant., Tox. Mat. News 1(13): 100-101 (1974).

Estimated costs for the vinyl chloride monomer (VCM) industry to meet a less than 10 ppm VCM level, and 1 to 5 ppm time-weighted average, will amount to 0.42¢/lb; a 50 ppm level will add .073¢/lb. In the polyvinyl chloride industry, estimates range from 0.72¢/lb to meet a 50 ppm VCM ceiling to 2.73¢/lb to meet a 25 ppm VCM ceiling with a 10 to 15 ppm time-weighted average. Protective clothing costs range from \$3.50 for a disposable suit to \$178.00 for a pressurized work suit with air tank. Monitoring equipment will average \$100,000 with operating expense of \$80,000 yearly plus up to \$20,000 for employment of a chemist. Total annual cost for medical examinations based on NIOSH recommendations will amount to \$160 per employee.

#### OCCUPATIONAL EXPOSURE; HUMAN; DIAGNOSTIC; STANDARDS; ECONOMICS

<11>

Anonymous, Vinyl chloride and cancer., Brit. Med. J. 1(5908): 590-591 (1974).

This editorial reviews some of the current literature relating angiosarcoma of the liver and vinyl chloride. Both human epidemiology and animal experimental data substantiate the causal relationship. Industrial cancer may become a recurrent problem until both old and new substances are screened. Feasibility of examining commercial substances for carcinogenesis is limited however because of 1) lack of trained personnel and facilities, 2) expense of animal tests, and 3) presence of disparities which in themselves could be carcinogenic.

#### REVIEW; OCCUPATIONAL EXPOSURE; HUMAN; CANCER; ANGIOSARCOMA; CASE REPORT

<12>

Anonymous, Vinyl chloride - the drive to reduce employee risks., Chemosology (Sept. 5, 1974).

Vinyl chloride (VC) and polyvinyl chloride producers have reported to the Occupational Safety and Health Association that a zero VC exposure level is unrealistic with present technology. Industry is operating under a 50 ppm limit until a permanent

standard is announced on October 5, 1974.

Manufacturing operations are separated by distance for safety reasons; therefore, the emissions problem is spread over a large plant-site. Wearing respirators full-time is neither safe nor feasible. "Corrective actions underway include installation of 1). Sequential monitoring systems that will constantly record vinyl chloride levels in all areas; 2). Organic vapor analyzers to detect minute leaks; 3). Improved pumps that reduce leakage; 4). Better ventilation systems; 5). Cleaning equipment that reduces the need for workers to enter reactors, and 6). Manifold systems to supply respirators during emergencies." Content of VC in polyvinyl chloride is being lowered. Automated, closed systems with computer controls to lower VC levels are being installed at a new plant, but actual levels will not be known until mid-1975 when production begins.

#### OCCUPATIONAL EXPOSURE; HUMAN; STANDARDS

<13>

Anonymous, Vinyl chloride., Hygienic Guide Series July-August (1964).

Reviewed briefly are hygienic standards, toxic properties, industrial hygienic practice, and emergency medical treatment. Recommended maximal atmospheric concentration of vinyl chloride for 8 hour exposure is 500 ppm. Based on 5-minute exposure studies with humans, 15,000 ppm produced varying degrees of intoxication with lightheadedness, nausea, dizziness, and dulling of visual and auditory acuity. Anaesthesia was the only significant effect of vinyl chloride in human inhalation studies, but it was an irritant to both skin and eyes. Fire and explosion are major industrial hazards.

#### HUMAN; RAT; MICE; GUINEA PIG; TOXICITY; INDUSTRIAL HYGIENE; SAFETY; EXPLOSIVE; STANDARDS; PROPERTIES; REVIEW

<14>

Anonymous, We produced over 13 million tons of resin in '73? Where is it? How about '74?, Modern Plastics 51(1): 36-47 (1974).

The United States plastics industry grew by 100% in the seven-year period 1967-1973. Polyvinyl chloride (PVC) held the third largest market in 1973, exceeded only by polyethylene and polystyrene. Building and construction industries were the largest consumers of PVC, with conduits, flooring, electrical wiring, and furniture using approximately 1/2 of the total produced. Producers were plagued in late 1973 by feed stock shortages, the oil embargo, high foreign prices, Phase IV controls, black markets, and a depressed building industry.

#### MANUFACTURE; ECONOMICS

<15>

Anonymous, Polyvinyl chloride banned in Japan., JAMA 229(7): 855 (1974).

Vinyl chloride has been banned as a propellant for aerosol insecticides and foricides by the Ministry of Health and Welfare of Japan. All products containing the monomer have been recalled. Vinyl chloride is suspected of being carcinogenic to the liver, and an immunological reaction has also developed in some people.

#### AEROSOLS; CANCER; LIVER

<16>

Anonymous, Cancer and vinyl chloride., JAMA 228(6): 684 (1974).

Any physician who has encountered patients suffering from angiosarcoma of the liver in the last 10 years is urged to contact the Center for Disease Control, Bldg 1, Room 520, Atlanta, GA, 30333 (Telephone 404

<16> CONT.  
633-3311, Ext. 3961). A surveillance registry has been established there by the National Institute for Occupational Safety and Health and the Bureau of Epidemiology of the Federal Center for Disease Control for aiding in epidemiologic studies of the possible relationship between hepatic angiosarcoma and exposure to vinyl chloride.

EPIDEMIOLOGY; OCCUPATIONAL EXPOSURE; ANGIOSARCOMA; LIVER

<17>  
Anonymous, Vinyl chloride., Matheson Gas Data Book, Matheson Co., Inc. 4th ed.: 489-492 (1966).

Vinyl chloride (VC) is less harmful than chloroform and carbon tetrachloride and is similar in toxicity to ethyl chloride. VC causes dizziness as a warning, except in very high concentrations, which cause almost immediate helplessness. In such a case, a physician should be summoned immediately, and the patient should be removed to an uncontaminated, well-ventilated room where the patient can be kept quiet and comfortably warm but not hot. In case of skin contact contaminated clothes should be removed, and the affected area washed with copious quantities of water, followed by soap solution. Eyes should be irrigated with copious quantities of water for at least 15 minutes, with the eyelids held apart during the irrigation to insure contact of the water with all tissues of the eyes and lids. An eye specialist should be consulted.

EYE; SKIN; MARCOSIS; THERAPY

<18>  
Anonymous, Vinyl chloride., Manual of Hazardous Chemical Reactions, National Fire Protection Assoc., Boston, Mass. 491A: 282 (1971).

Vinyl chloride is oxidized by atmospheric oxygen in the presence of any of a variety of contaminants to an unstable polyperoxide which increases under storage to hazardous levels. Manufacturing Chemists' Association Case History 1551 in 1969 is cited.

SAFETY; EXPLOSIVE

<19>  
Anonymous, Epidemiologic notes and reports: Angiosarcoma of the liver among polyvinyl chloride workers--Kentucky, Morbidity and Mortality Weekly Report, Center for Disease Control, Atlanta, Ga. 23(6): 49-50 (1974).

Four cases of angiosarcoma of the liver were diagnosed among male employees of a polyvinyl chloride polymerization plant near Louisville, KY. All had worked continuously in the polymerization process for at least 14 years prior to illness. Pathologic examination revealed extensive non-alcoholic cirrhosis in addition to angiosarcoma in all 4 cases. The possibility of a work-related carcinogen, conceivably vinyl chloride, is being studied.

ANGIOSARCOMA; CASE REPORT; OCCUPATIONAL EXPOSURE; EPIDEMIOLOGY; MORTALITY

<20>  
Anonymous, Tracking down a carcinogen., MD (Medical News) 18(8): 49-51 (1974)

Vinyl chloride (VC) was first used in manufacturing plastics in the 1930s. Soviet researchers noted liver damage in 25% of VC workers in 1949. A threshold limit of 500 ppm was established in the USA and was not changed despite demonstration by Dow Chemical Company in 1961 that 50 ppm caused liver damage in animals. Acroosteolysis of the hands and feet was observed in the 1960s in France and Great Britain and in the Goodrich plant in the USA. In

1970 Dr. P.L. Viola in Rome found that rats exposed to high concentrations of VC developed cancers, which was verified by Dr. C. Maltoni of the University of Bologna. Dr. Maltoni notified the Manufacturing Chemists Association in 1972 but no action was taken. In January 1974, B.F. Goodrich made public the death of 4 VC workers from angiosarcoma of the liver, thought to be caused by VC. The Environmental Science Laboratory, headed by Dr. I.J. Selikoff, immediately organized a 17-member team, which by midsummer had already given detailed examinations to over 1200 VC workers. Hepatic fibrosis, which may possibly precede angiosarcoma, is difficult to diagnose, but an experimental bile acid clearance test may be helpful. Lung function tests showed obstructed airways in 80% of men with 20 yrs exposure. Since VC is used as a propellant in aerosols, these products have been recalled or the sale banned. EPA has detected VC in air measurements, and urged reduction of these air levels. The Labor Department set a temporary level of 50 ppm in workrooms, but manufacturers want a gradual reduction in the standard to reach a daily average of 10 ppm by October 1976.

STANDARDS; ANGIOSARCOMA; OCCUPATIONAL EXPOSURE; AEROSOLS; ANALYSIS; ACROOSTEOLYSIS

<21>  
Anonymous, Labels and code numbers of products containing vinyl chloride recalled by manufacturers., Food and Drug Administration Press Release 74-23. 12 pages (April 3, 1974).

The Food and Drug Administration initiated action on April 3, 1974 to insure that vinyl chloride (VC) is not used in any aerosolized food, drug, or cosmetic product. Use of VC in aerosol products regulated by FDA is minimal, and FDA is unaware of its use in any food product, or in any aerosolized cosmetic or drug product at present. Manufacturers who previously used VC as a propellant are requested to withdraw the products still on the market. Manufacturers are requested to identify products containing VC, and a listing of such products, with their code numbers is appended. A ban is proposed for PVC as a packaging material for alcohol-containing food or beverages and PVC containers for other food are under investigation.

AEROSOLS; COSMETIC; DRUG; REGULATION

<22>  
Anonymous, Vinyl chloride, P.V.C., and cancer., Lancet 1(7870): 1323-1324 (1974).

A vinyl-chloride-related case of angiosarcoma in England is cited. The Department of Employment Factory Inspectorate has set an interim upper limit for exposure to vinyl chloride (VC) with maximum time-weighted average exposure of 25 ppm. Manufacturers have pooled experience and resources in a guidance document for polyvinyl chloride (PVC) producers. The amount of unreacted VC which might be released from PVC in storage, during heating, during compounding, in fabrication processes, or from food packaging is unknown. All cases of angiosarcoma known to date resulted from 12 to 27 years exposure in PVC manufacturing plants. Discovery of health hazards has resulted in efforts to protect employees. The current VC episode is a milestone in industrial hygiene which must result in a more systematic evaluation of industrial chemicals for carcinogenic risk to workers.

OCCUPATIONAL EXPOSURE; ANGIOSARCOMA; CANCER; STANDARDS

<23>  
Anonymous, Vinyl chloride., Chem Sources - U.S.A., Directories Publishing Co., Inc., Pleasanton, W.J. (1974).

Listed sources of vinyl chloride in the United States in 1974 are: Allied Chemical Corp.; American Chemical Corp.; Air Products and Chemicals, Inc.;

<23> CONT.

B.F. Goodrich Chemical Co.; Borden Chemical; Continental Oil Co.; Diamond Shamrock Corp.; Dow Chemical Co.; Ethyl Corp.; Goodyear Tire & Rubber Co.; Matheson Gas Products; Precision Gas Products, Inc.; PPG Industries; Scientific Gas Products of New England; Scientific Gas Products; Shell Chemical Co.; Tenneco Chemicals, Inc.; Union Carbide Corp.; Unifroyal Chemical.

#### MANUFACTURE

<24>

Anonymous, More facts on vinyl chloride and cancer., Brit. Med. J. 4(5943): 486-487 (1974).

Vinyl chloride (VC) is now known to induce tumors in man, and has been shown in animals to cause cancer at exposures of 50 ppm, 4 hr/day, 5 days/wk. VC has caused tumors in animal tissues other than the liver, but has not yet been proven to do so in man. Concentrations of 1 to 2 ppm VC have been found in ambient air near factories producing VC; 200 to 400 ppm may be present in manufactured polyvinyl chloride (PVC); 0.5 to 20 ppm in processed PVC plastic; and small amounts may be transferred into food from PVC packaging or into water through PVC pipes. Potential and real hazards to the general population through these low exposures, and the possibility of human tumors other than angiosarcoma of the liver, must be determined.

NON-OCCUPATIONAL EXPOSURE; RAT; MICE; HUMAN; CARCINOGENICITY

<25>

Anonymous, Angiosarcoma of the liver in vinyl chloride/polyvinyl chloride workers., J. Occup. Med. 16(2): 809 (Dec. 1974).

Members of the medical community in the United States and abroad are requested to report information on known or suspected cases of angiosarcoma of the liver to Dr. J. W. Lloyd, Director, Office of Occupational Health Surveillance and Biometrics, NIOSH, 5600 Fishers Lane, Room 3-32, Park Building, Rockville, MD, 20852. Twenty-six cases have been reported to date from 6 countries: Sixteen from the United States; 2 Czechoslovakia; 2 Great Britain; 1 Norway; 2 Sweden; 3 W. Germany. Cases have been reported from 4 distinct work areas, but 81% had worked as reactor cleaners. The median interval from first exposure to diagnosis is 20 years.

EPIDEMIOLOGY; ANGIOSARCOMA; CASE REPORT

<26>

Antonyuzhenko, V.A., Occupational vinyl chloride poisoning., Gig. Tr. Prof. Zabol. 12: 50-52 (1968).

Manifestations of poisoning by vinyl chloride exhibit generally three phases. Only at the first phase, in which osteoporotic and osteosclerotic symptoms appear, is the disease fully reversible after discontinued contact with the toxic factor. The second phase is not easily characterized, but there is a higher involvement of the involuntary nervous system, with disturbances in volition and motivation. Vascular paroxysms acquire a 2-phase character, changing from spasms to atonic, and there may be cardiac arrhythmia, systolic disturbances, and pain in the heart region. Stage 3 is characterized by depression, hallucinations, insomnia, and speech and eye disturbances as diagnostic indications of primary disease of the brain stem.

Russ.

BRAIN; NEUROLOGICAL; CARDIOVASCULAR; TOXICITY

<27>

Arena, J.M., Infrared analysis of gases and vapors in expired air., Poisoning. Charles C. Thomas,

Springfield, Illinois 2nd ed., 66-67 (1970).

Breath analysis is a rapid analytical method for diagnosis of solvent poisoning or exposure. It is sufficiently sensitive to permit detection hours to weeks after excretion, depending on amount absorbed, rate of metabolism, and rate of excretion. An excretion curve after exposure is compared to a controlled excretion curves to arrive at an estimation of total amount absorbed. An infrared sensitivity of 10 ppm vinyl chloride in post-exposure expired air is noted, but 5 to 10 times this amount must be present to obtain a positive identification. The infrared analytical wavelength is 10.63 microns. Vapor phase chromatographic sensitivity to vinyl chloride was 0.1 ppm.

#### ANALYSIS

<28>

Aviado, D.M.; Belej, M.A., Toxicity of aerosol propellants on the respiratory and circulatory systems. I. Cardiac arrhythmia in the mouse., Toxicology 2: 31-42 (1974).

Fifteen propellants used in aerosols were investigated in anesthetized mice, and grouped into three classes according to their toxicity. The propellants of Class I, in which vinyl chloride (VC) is included, induce arrhythmia in the mouse and sensitize the heart to epinephrine in both the mouse and dog. A 5% concentration of VC sensitized the heart of unanesthetized dogs to epinephrine. Ten percent was required to sensitize the anesthetized mouse to epinephrine, and 20% to induce arrhythmia in the mouse. Class I propellants are assessed as dangerous, and their continued use in aerosols is questioned.

AEROSOLS; HUMAN; MICE; DOG; CARDIOVASCULAR

<29>

Baretta, E.D.; Stewart, R.D.; Mutchler, J.E., Monitoring exposures to vinyl chloride vapor: Breath analysis and continuous air sampling., Amer. Ind. Hyg. Assoc. J. 30: 537-544 (1969).

An environmental survey, featuring continuous multipoint air sampling and analysis using an infrared spectrophotometer, was conducted to determine the time-weighted average exposure (TWA) of a group of chemical plant workers to vinyl chloride vapor. Concurrently, a breath sampling program resulted in a series of derived breath decay curves relating post-exposure breath concentration to vapor exposure. Results achieved from the two methods suggest that either continuous air monitoring or breath analysis is valid for estimating a worker's individual daily exposure to vinyl chloride. Breath analysis is a useful technique for evaluating vapor exposure.

OCCUPATIONAL EXPOSURE; HUMAN; ANALYSIS

<30>

Barr, R.F.; Watts, R., Diffusion of some organic and inorganic compounds in air., J. Chem. Eng. Data 17(1): 45-46 (1972).

Diffusion coefficients in air for several compounds including vinyl chloride (VC) were determined at 298.2 degrees K and 1 atmosphere by means of an infrared absorption cell fitted with a side capillary open to the atmosphere, and placed in the beam of an infrared spectrophotometer. Vinyl chloride with a coefficient of 0.1225 plus or minus 0.0053 had a deviation larger than the average of the group, mainly because the frequency of the infrared peak used to follow the VC was in the water region of the spectrum (1620), and relative humidity in the laboratory ranged from 43-56%.

#### PROPERTIES

<31>

Barr, R.J.; Bonin, M., Polyvinyl Chloride: Letter to the Editor., JAMA 231(9): 914 (1975).

In a case of proven primary hemangiosarcoma of the liver, a stain for acid mucopolysaccharides (Alcian blue; pH, 2.5) gave strongly positive results in sections taken from the liver. This is consistent with an increase in the production of sulfated mucopolysaccharides (chondroitin sulfate A, B, C). Quality and quantity of acid mucopolysaccharides in neoplasms, serum and urine of those at risk could be of value in screening tests.

DIAGNOSTIC; CARCINOGENICITY; LIVER; LETTER

<32>

Basalava, A.V., (Experience with the use of large-frame photofluorography in examining skeletal bones of persons occupationally dealing with unsaturated hydrocarbons of the ethylene series (olefins) and their chlorine derivatives (vinyl chloride, trichloroethylene).), Gg. Tr. Prof. Zabol. 14(1): 34-37 (1970).

Persons occupationally exposed to chlorinated hydrocarbons of the ethylene series, including vinyl chloride, revealed definite skeletal alterations in bones, e.g., osteosclerosis, osteoporosis, osteolysis. Diagnosis using large-frame photofluorography is recommended because of the lesser radiation load.

Russ.; Eng. Sum.

HUMAN; CASE STUDY; PHOTOFLUOROGRAPHY; OSTEOLYSIS; OSTEOSCLEROSIS; OSTEOPOROSIS; OCCUPATIONAL EXPOSURE; DIAGNOSTIC

<33>

Basalava, A.V.; Vazin, A.M.; Kochetkov, A.G., (Pathogenesis of changes developing due to long-term exposure to vinyl chloride.), Gg. Tr. Prof. Zabol. 16(2): 24-27 (1972).

Changes in the bioelectric activity of the hypothalamus, hyperadrenalinemia, resorption of bone tissue, osteoporosis, and functional troubles of the cardiovascular system occurred in rats and rabbits inhaling 0.03-0.04 mg/l vinyl chloride fumes 8 hr a day for 6 months. Dysfunction of the hypothalamus apparently gives rise to neurohumoral and neurovascular disturbances which lead to development of dystrophic processes in bone tissue.

Russ.; Eng. Sum.

HYPOTHALAMUS; BONE; NEUROLOGICAL; CARDIOVASCULAR; RAT; RABBIT

<34>

Bastien, R.; Cordier, J.M.; Lefevre, M.J., Acro-osteolysis, occupational., Encyclopaedia of Occupational Health and Safety 1: 33-34 (1971).

Fifty cases of occupational acroosteolysis, of which 30 were in the USA, have been reported among workers employed in removing deposits from the walls of polyvinyl chloride polymerization vessels. The mechanism of the syndrome is unknown, but causative factors are: a chemical insult, a physical insult, and a personal reactivity. All cases have 2 symptoms in common in varying degrees - Raynaud's phenomenon, and skeletal changes of the extremities, particularly the distal phalanges of the fingers. Evidence of collagen disease, osteolysis, or abnormal response of hands to cold should contraindicate employment as a polycleaner. Cessation of polycleaning work allows spontaneous healing, but no other treatment has been found effective.

POLYCLEANER; OCCUPATIONAL EXPOSURE; ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON

<35>

Berk, P.D.; Martin, J.F.; Waggoner, J.G., Persistence of vinyl chloride-induced liver injury after cessation of exposure., Ann. N.Y. Acad. Sci. 246: 70-77 (1975).

A white male employed for 5 1/2 yrs as an autoclave cleaner before a splenectomy and a liver biopsy showed portal fibrosis and histologic abnormalities. This case report represents a unique follow-up of apparent vinyl chloride-induced liver injury 2 1/2 yrs after removal from exposure. The case was evaluated by the National Institutes of Health, and special studies, directed toward finding a suitable screening test of liver function which would reflect histologic abnormalities, were performed. The detailed evaluation indicates that hepatic fibrosis persists and may progress despite removal from further exposure. Because of the nature of the hepatic injury, the lesion may be extensive but may not be revealed by abnormal results of standard liver function tests.

LIVER; LONG; DIAGNOSTIC; OCCUPATIONAL EXPOSURE; HUMAN; CASE REPORT

<36>

Block, J.B., Angiosarcoma of the liver following vinyl chloride exposure., JAMA 229: 53-54 (1973).

Case studies of six employees who had worked for at least 12 years with vinyl chloride are presented. The extremely rare angiosarcoma of the liver was diagnosed in all 6 cases. Four cases showed an unusual type of cirrhosis.

CASE REPORT; CASE STUDY; OCCUPATIONAL EXPOSURE; ANGIOSARCOMA; CIRRHOSIS; HUMAN; EPIDEMIOLOGY

<37>

Boettner, E.A.; Weiss, B., An analytical system for identifying the volatile pyrolysis products of plastics., Amer. Ind. Hyg. Assoc. J. 28(1): 535-540 (1967).

For identifying and quantifying the pyrolytic products of certain synthetic resins when heated in air, a system of instrumental analysis makes use of differential thermal analysis to determine the temperature at which physical and chemical changes occur in the plastic, and thermogravimetric analysis for determining the temperature at which it undergoes weight losses. Compounds liberated at the decomposition temperatures are either analyzed directly by infrared absorption spectroscopy, mass spectroscopy, or gas chromatography, or are collected in fractions through use of a combustion furnace and separated further through gas chromatography. Application of the analytical system to polyvinyl chloride is described.

ANALYSIS

<38>

Bol'shakov, A.M., (Hygienic evaluation of working conditions in the synthetic leather industry.), Gg. Vop. Proizvod. Priem. Polim. Mater. 1969: 47-52 (1969). (CA75: 143701p)

At certain locations in an artificial leather manufacturing plant vinyl chloride concentrations reached 0.06 mg/m<sup>3</sup>. Employees experienced a general reduction in muscular strength, absenteeism was unusually high, and many operators reported periodic pains in feet and hands. Of 127 workers examined, 38 showed vegetative polyneuritis effects.

Russ.

OCCUPATIONAL EXPOSURE; STANDARDS; NEUROLOGICAL

<39>

Breder, C.V.; Denslow, J.L.; Brown, M., Investigation of some GLC procedures for vinyl chloride monomer in polyvinyl chloride, food, and

R&S 135404

<39> CONT.  
food simulants., J. Assoc. Offic. Anal. Chem. To be published.

Preliminary studies are described for the determination of vinyl chloride monomer in polyvinyl chloride, food, and food-simulating solvents. Topics discussed include: Problems in preparation of standards, GLC columns, detectors and operating parameters, techniques for achieving rapid GLC turn around time, interferences and their elimination. (Author Abstract).

#### ANALYSIS

<40>  
Bridbord, K.; Brubaker, P.; Gay, B.; French, J., Exposure to halogenated hydrocarbons in the indoor environment., Environ. Health Perspect. 11: 215-220 (1975).

Halogenated hydrocarbons from aerosol products may contribute to levels of indoor air pollution which are a public health concern. Aerosols containing vinyl chloride as a propellant is one of the documented examples. Contamination of the outdoor environment by halogenated hydrocarbons may also be a factor in the contamination of indoor air spaces, and should be carefully examined.

#### NON-OCCUPATIONAL EXPOSURE; HUMAN; AEROSOLS

<41>  
Burgess, R.R.; Greaves, J.C., Deposition prevention in vinyl chloride polymerization., Ger. Offen. 2,357,869 (Imperial Chemical Industries, Ltd.) 18 pp (30 May, 1974). (CA 81: 78540t)

Deposits on the walls of the reactor vessel during polymerization of vinyl chloride (VC) were prevented by coating the reactor with cross-linked formaldehyde polymers such as formaldehyde-ethyleneimine copolymers prior to the aqueous suspension polymerization process. The British processor claims no deposits, as compared to 0.015 parts of deposit/100 parts vinyl chloride with untreated walls.

#### PATENT; SYNTHESIS

<42>  
Burgess, R.R.; Tomlinson, R.W.M., Deposition prevention in vinyl chloride polymerization., Ger. Offen. 2,357,867 (Imperial Chemical Industries, Ltd.) 16 pages (30 May, 1974). (CA 81: 78539x.)

Aqueous suspension polymerization of vinyl chloride (VC) at pH<sup>4</sup> in the presence of 1000 ppm polyethyleneimine was accomplished without deposition on the walls of the reactor vessel.

#### PATENT; SYNTHESIS

<43>  
Byren, D.; Holmberg, B., Two possible cases of angiosarcoma of the liver in a group of Swedish vinyl chloride-polyvinyl chloride workers., Ann. N.Y. Acad. Sci. 246: 249-250 (1975).

In Sweden, around 620 workers are employed in one polyvinyl chloride (PVC) polymerization plant and one vinyl chloride (VC) synthesizing plant. Both began operation in 1945, but no measurement of exposure was made before 1968 when hygienic conditions were greatly improved to reach 18-20 ppm in reactor rooms and under 5 ppm in drying and packing departments. The first case reported is that of a reactor operator employed for 18 yrs before appearance of disease at age 49. Symptoms presented were loss of weight, spleno- and hepatomegaly, anemia, moderate elevation in erythrocyte sedimentation rate, greatly elevated alkaline phosphatase, and slightly elevated GPT. Angiography confirmed liver tumor, and cytologic examination indicated primary hepatocellular cancer.

At postmortem, the tumor was diagnosed as low differentiated primary liver carcinoma. Case 2 was employed in VC production for 23 yrs and for 4 more yrs at very low exposures before appearance of the disease at age 61. Symptoms included epigastric tumor, thrombocytopenia, and slightly elevated alkaline phosphatase, transaminases, and lactic dehydrogenase. Angiography revealed tumor masses in a grossly enlarged liver, malignancy was confirmed by biopsy, and postmortem diagnosis was primary hepatocellular carcinoma. Recent specialized examination has confirmed a diagnosis of hemangiosarcoma in both cases, with probable coexistence of a hepatocellular cancer in Case 2.

#### CANCER; ANGIOSARCOMA; CASE REPORT; HUMAN

<44>  
Capurro, P.U.; Gray, R.L., Need for research for protective measures against chronic chemical injury., JAMA 229(7): 761-764 (1974).

Several years of exposure to industrial chemicals may occur before malignant neoplasia can be detected. Studies of patients exposed to solvent vapors indicated damage to liver and pancreas before a definite increased rate of malignancy was noted. A 30-yr old man who had cleaned vinyl chloride storage tanks for four years complained of great fatigue. Scans of the liver showed it to be small with an irregular concave profile; scans of the pancreas had an abnormally low count and uneven isotope uptake. Glucose tolerance and insulin curves were abnormal. These findings were common in people exposed to solvents. A study of trace minerals may be of value in helping to control damage to liver and pancreas. Protection against chemical exposure will require cooperation from physicians, labor unions, and plant managers.

#### LIVER; CANCER; OCCUPATIONAL EXPOSURE

<45>  
Caputo, A.; Viola, P.L.; Bigotti, A., Oncogenicity of vinyl chloride at low concentrations in rats and rabbits., ICRS Library Compendium (International Research Communication System) 2: 1592 (1974).

The carcinogenic effect of vinyl chloride in almost all tissues and organs was confirmed in experiments with 1100 rats exposed for 3 hrs/day, 5 days/week, for 12 months to a flow of air containing 20,000, 10,000, 5,000, 2,000, 500 or 50 ppm vinyl chloride. All concentrations except the lowest produced neoplasms in different organs and tissues, with prevalence of the liver. In experiments with other animals, tumors similar to those described in rats appeared. In particular, the rabbit displays a high sensitivity to vinyl chloride.

#### RAT; CARCINOGENICITY

<46>  
Carr, C.J.; Burgison, R.M.; Vitcha, J.P.; Krantz, J.C., Anesthesia XXIV. Chemical constitution of hydrocarbons and cardiac automaticity., J. Pharmacol. Exp. Ther. 97(1): 1-3 (1949).

Gaseous compounds, including vinyl chloride, in concentrations from 15 to 90%, were administered to dogs who had previously been injected with epinephrine HCL, 0.01 mg/kg. Closed circuit inhalation was continued from 10 to 20 minutes, then repeated. In 3 of 7 dogs inhaling vinyl chloride, sensitization of the myocardium occurred. Myocardial sensitization occurred less frequently with vinyl chloride than with its saturated analog, ethyl chloride. Failure to sensitize was a matter of degree and not an absolute absence of some incipient effect. No correlation was possible between observations made and the physical properties of saturated or unsaturated hydrocarbons.

#### DOG; NEUROLOGICAL; PROPERTIES; ANESTHETIC

<47>  
Chatelain, A.; Motillon, P., Un syndrome d'acro-osteolyse d'origine professionnelle et de constatation nouvelle en France. (A syndrome of acroosteolysis of occupational origin of recent observation in France.), Radiol., Electrol. 48(5): 277-280 (1967).

Five cases in a population of 103 persons exhibited acroosteolysis with Raynaud's syndrome presumably of occupational, and probably of toxic origin. All were cleaners of autoclaves used in the polymerization of vinyl chloride. Nine other cases of Raynaud-type syndrome without bony lesions, and 14 cases of simple sensitivity to cold were observed. Could these signs represent the onset of the disease? Three hundred and thirty-eight workers who manipulated the polymer after autoclaving were found radiologically free of all lesions.

Fr.

OCCUPATIONAL EXPOSURE; HUMAN; BONE; RAYNAUD'S PHENOMENON; ACROOSTEOLYSIS; EPIDEMIOLOGY; CASE STUDY

<48>  
Chenoweth, M.B.; Hake, C.L., The smaller halogenated aliphatic hydrocarbons., Annu. Rev. Pharmacol. 2: 381 (1962).

This extensive review considers the literature from 1955 to June 1961 on compounds containing from 1 to 4 carbon atoms and 1 or more halogen atoms. The effects of vinyl chloride in mice, rats, and guinea pigs were investigated by Danziger and coworkers after 2 accidental deaths in the polyvinyl chloride industry. Principal pathological changes noted were congestion in the lungs, liver and kidneys, pulmonary edema and hemorrhage, and failure of the blood to clot. These results tended to confirm the cause of death in the human overexposure. The work of Rockelson and colleagues indicated that concentrations of vinyl chloride of more than 50 ppm were deleterious to rats, rabbits, guinea pigs, and dogs. The review concludes that the accepted threshold limit of 500 ppm is too high.

TOXICITY; OCCUPATIONAL EXPOSURE

<49>  
Christensen, H.E., Ed., Chloroethylene, Toxic Substances List, National Institute for Occupational Safety and Health, Rockville, MD. p 350 (1974).

Listed synonyms for vinyl chloride include: chloroethene, Trovidur, Vinyl C Monomer, and vinyl chloride. Chemical Abstracts Registry number is 75014, and Weissesser Line Notation is G101. The lowest concentration at which toxic effects (cardiovascular) were found from inhalation of vinyl chloride by humans is 20 ppm. In the rat, 250 ppm exposure for 4 hr/day for 260 days was the lowest lethal concentration, which also acted as a carcinogen. In the mouse, 500 ppm exposure for 4 hr/day for 30 weeks was the lowest lethal concentration, also with carcinogenic effects. The U.S. time-weighted-average Standard is 500 ppm. An emergency Standard of 50 ppm was set in 1974.

STANDARDS; OCCUPATIONAL EXPOSURE; RAT; MICE; HUMAN; CARDIOVASCULAR; CANCER

<50>  
Cohan, G.F., Industrial preparation of polyvinyl chloride., Environ. Health Perspect. 11: 53-57 (1975).

Vinyl chloride (VCM) is unloaded from tank cars (rail or truck) into pressurized storage spheres. Watered VCM, emulsifiers, and catalysts are then reacted in an aqueous medium in polymerization vessels under controlled conditions of temperature and pressure. These contents are transferred to a secondary vessel where steam is injected, and the VCM-containing vapors are pumped to a recovery system where the vapors are compressed, cooled,

condensed, decanted, and recycled for reuse. Batches of the PVC resin water slurry are blended for product uniformity, and then a dewatering centrifuge removes approximately 90% of the water, which is discharged to the industrial sewer system. Remaining water is removed in a flash dryer and the dry resin enters a two-stage collection system for separation of conveying air. The PVC resin is then screened, and stored to be later shipped, compounded, or bagged.

MANUFACTURE

<51>  
Cook, V.A.; Giever, P.M.; Dinsan, S.D.; Haganson, R.J., Occupational acroosteolysis. II. An industrial hygiene study., Arch. Environ. Health 22: 74-82 (1971).

An industrial hygiene investigation for acroosteolysis (AOL) was conducted in 32 plants engaged in the handling of vinyl chloride. Identification of variables in processes and chemicals which were peculiar to plants having known cases of AOL was the objective. No unique situations were shown to exist. A correlation of AOL cases with manual reactor-cleaning methods was observed. A number of situations relating to a precise cause of AOL require additional exploration.

OCCUPATIONAL EXPOSURE; ACROOSTEOLYSIS; POLYCLEANER; INDUSTRIAL HYGIENE; EPIDEMIOLOGY

<52>  
Corn, M., Discussion paper (Control and management), Ann. N.Y. Acad. Sci. 246: 303-305 (1975).

Equations for the calculation of pollutant concentration in a workroom are presented and discussed. Ventilation approaches to the control of toxic materials are standard, and although it is not possible to design to a specified Threshold Limit Value (TLV), sufficient design options exist to ensure control for highly toxic materials. Past designation of vinyl chloride as a low toxicity material encouraged a less controlled design of ventilation, but future design will be for a highly toxic material with techniques appropriate to this designation.

INDUSTRIAL HYGIENE; STANDARDS; OCCUPATIONAL EXPOSURE

<53>  
Creech, J.L.; Johnson, M.W., Angiosarcoma of liver in the manufacture of polyvinyl chloride., J. Occup. Med. 16(3): 150-151 (1974).

Three fatal cases of angiosarcoma of the liver occurred within a period of approximately two years among the employees of a polyvinyl chloride manufacturing plant. Since all 3 were treated by different physicians, no relationship to polyvinyl chloride was surmised until the authors recognized the rarity of the disease and learned that all 3 men had worked in the same plant. One case report is presented. History, pathology, and clinical course are consistent with the other two who died of angiosarcoma. Clinical, epidemiologic, toxicological, and occupational investigations are now being vigorously pursued with regard to other employees.

CASE REPORT; OCCUPATIONAL EXPOSURE; HUMAN; ANGIOSARCOMA; LIVER

<54>  
Creech, J.L.; Math, L., Liver disease among polyvinyl chloride production workers., Ann. N.Y. Acad. Sci. 246: 88-94 (1975).

In an attempt to relate liver abnormality to vinyl chloride (VC) exposure in the B.F. Goodrich chemical plant in Louisville, Ky, five categories were determined: The highest exposure is in 1) polyvinyl chloride production; followed in order of exposure

## &lt;54&gt; CONT.

by 2) other production, including the rubber plant, 3) maintenance of polyvinyl chloride production, 4) all other maintenance, 5) all other employees. A series of tests to determine extent of liver disease in vinyl chloride workers was initiated, with a predetermined protocol of testing to be followed when abnormalities appeared. Two additional cases of angiosarcoma have been found and 11 cases of portal fibrosis, 2 of which were not in polyvinyl chloride production. Fifty-nine employees were moved to areas of no exposure to known hepatic toxins. The studies will continue throughout employment life, and perhaps after retirement.

DIAGNOSTIC; LIVER; OCCUPATIONAL EXPOSURE; CASE REPORT

## &lt;55&gt;

D'yachuk, I.A., (A contribution to the hygienic evaluation of PVC floor tiles for apartments.), Gig. Sanit. (Hyg. Sanit.) 35(1-3): 424-427 (1970).

Toxic substances released from polyvinyl chloride (PVC) floor tiles were investigated in both the laboratory and in apartments with PVC floors. Air was sampled for volatile substances at heights of 0.5 and 1.5 m above floor level at 9, 11, and 14 months after the floors were laid. Vinyl chloride was determined titrimetrically. Physiological effects on the apartment dwellers were determined by questioning, blood pressure, and pulse. In contrast to occupants of apartments without PVC tiles, noticeable signs and symptoms included irritated mucosae of the respiratory tract, low blood pressure, bradycardia, dizziness, loss of appetite, irritability, and wakefulness during the night. In general, vinyl chloride concentrations were higher at the lower sampling height. In one room, for example, 0.388  $\mu\text{g}/\text{m}^3$  was detected at the 0.5 m level whereas 0.193  $\mu\text{g}/\text{m}^3$  was found at the 1.5 m height. Levels decreased with time. PVC tiles were not recommended in hot, dry climates.

Russ.; Eng. Transl.

INDUSTRIAL HYGIENE; HUMAN; DEGRADATION;  
DEPOLYMERIZATION; EPIDEMIOLOGY; NEUROLOGICAL;  
GASTROINTESTINAL; STANDARDS; CASE STUDY;  
NON-OCCUPATIONAL EXPOSURE

## &lt;56&gt;

Danilshvsky, S.L.; Egorov, M.M., (Problems of toxicology in the chemistry of high-molecular compounds.), Gig. Tr. Prof. Zabol. 5(9): 26-31 (1964).

Monomers, catalysts, and additives used in the synthesis of polymers are different both chemically and toxicologically. Monomers are generally reactive and biologically aggressive. Monomer toxicity may be increased by contaminants. Polymer toxicity may increase with an increase in temperature, and may be significant in the aging of the polymer. Proper hygienic standardization is important, both in the working conditions during synthesis and in the utilization of the products in the national economy.

Russ.; Eng. Summ.

OCCUPATIONAL EXPOSURE; NON-OCCUPATIONAL EXPOSURE;  
TOXICITY; STANDARDS

## &lt;57&gt;

Danziger, M., Accidental poisoning by vinyl chloride: Report of two cases., Can. Med. Assoc. J. 82: 828-830 (1960).

Two fatal cases in autoclave cleaners of accidental poisoning by vinyl chloride are reported. Autopsy findings in both were similar but could not be extrapolated for diagnostic purposes - other chemicals cause similar reactions. Pathology included cyanosis; local burns of conjunctivae and corneae; congestion of internal organs, especially lungs and kidneys; and failure of the blood to clot.

Circumstances proved one case to be caused by vinyl chloride whereas some doubt accompanies the other.

POLYCLINER; CASE REPORT; CASE STUDY; LUNG; KIDNEY;  
EYE; BLOOD

## &lt;58&gt;

Deichmann, W.B.; Gerarde, H.W., Vinyl chloride (chloroethylene; chloroethene). Toxicology of drugs and chemicals., Academic Press, New York Ch.4: 620-621 (1969).

Vinyl chloride is a colorless gas with a sweetish odor and little or no irritating effect. Six humans exposed to 4000 ppm for 5 min reported no effects; 12,000 ppm caused dizziness; 25,000 ppm caused disorientation as to space and size, and a burning sensation in the feet. Forty percent vinyl chloride caused death in 2 of 5 guinea pigs with congestion of the lungs, pulmonary edema, hemorrhages, and congestion of the liver and kidneys. Thirty-one cases among 3000 polyvinyl chloride workers exhibited hand disorders which included Raynaud's phenomenon, acroosteolysis, clubbing of the fingers, skin lesions, and a rope-like appearance resembling scleroderma.

REVIEW; HUMAN; GUINEA PIG; LUNG; LIVER; KIDNEY;  
RAYNAUD'S PHENOMENON; ACROOSTEOLYSIS; SKIN

## &lt;59&gt;

Derby, J.V.; Freedman, R.W., Vapor-phase pyrolysis and GC analysis of fire-retardant materials containing PVC., Amer. Lab. 6(5): 10-16 (1974).

In vapor-phase pyrolysis, which is useful for characterization and quantitative analysis of polymers, the products of rapid pyrolysis yield recorded traces called "pyrograms" when separated on chromatographic columns. These traces characterize the polymers by peaks identifiable by retention time, volume, Kovats indices, and other constants. To determine functional groups, major peaks are subjected to vapor-phase pyrolysis to yield small molecules such as  $\text{CO}_2$  or  $\text{CH}_4$ , which can be measured quantitatively by chromatography. Once the functional group of a molecule is established, identity can be determined from the ratio between retention time and carbon number. Reproducible pyrograms of polyvinyl chloride indicate vinyl chloride as a possible product of pyrolysis on the basis of retention time.

## ANALYSIS

## &lt;60&gt;

Dlaov, D.; Beritic, T., Profesionalna akroosteoliza. (Occupational acroosteolysis.), Arch. Hig. Rada Toksikol. (Arch. Ind. Hyg. Toxicol.) 22(1): 53-54 (1971).

A two-page review is presented on the series of 3 articles by Dinaan, et al; Cook, et al; and Dodson, et al on occupational acroosteolysis previously published in the Archives of Environmental Health in 1971.

Serbo-Croat

ACROOSTEOLYSIS; REVIEW

## &lt;61&gt;

Dinaan, B.D.; Cook, W.A.; Whitehouse, W.H.; Magnuson, H.J.; Ditchek, T., Occupational acroosteolysis. I. An epidemiological study., Arch. Environ. Health 22: 61-73 (1971).

In epidemiological study covering 5,011 employees with 21,510 man-years experience in various phases of vinyl chloride and polyvinyl chloride manufacturing exposed 25 definitive cases and 16 questionable cases of acroosteolysis (AOL). All were clearly associated with the hand cleaning of polymerizers. The disease appears to be systemic rather than local, and the importance of Raynaud's

## &lt;61&gt; CONT.

phenomenon as a concomitant is emphasized. Neither the etiological agent nor point of entry is known. Several statistical approaches for rapid medical survey are suggested.

EPIDEMIOLOGY; OCCUPATIONAL EXPOSURE; RAYNAUD'S PHENOMENON; ACROOSTEOLYSIS; STATISTICS; INDUSTRIAL HYGIENE

## &lt;62&gt;

Dodson, V.N.; Dinman, B.D.; Whitehouse, W.N.; Masr, A.W.M.; Magnuson, R.J., Occupational acroosteolysis. III. Clinical study., Arch. Environ. Health 22: 83-91 (1971).

Four subjects with osteolytic lesions, especially in the distal phalanges of the hands, were studied clinically. All had Raynaud's phenomenon which antedated the osteolytic lesions. All had worked as polycleaners in the polyvinyl chloride industry; hand scraping was common. Detailed medical and family histories, physical examinations, dietary and metabolic studies, and laboratory investigations were made. Numerous roentgenographic techniques were used. Plethysmography revealed abnormalities in three men, whereas esophageal motility was normal. The initial signs and symptoms suggesting acroosteolysis comprised blanching of the hands associated with either tingling of the hands or tenderness of the fingertips.

ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON; POLYCLEANER; OCCUPATIONAL EXPOSURE; CASE STUDY; BONE; BIOCHEMISTRY; INDUSTRIAL HYGIENE

## &lt;63&gt;

Doll, R., Discussion paper., Ann. N.Y. Acad. Sci. 246: 320-321 (1975).

The problem of extrapolation of data is an extremely complicated one. A particular chemical carcinogen is only one factor which interacts with a number of others, and a simple linear relationship with one factor may be seen in all sorts of complex situations. Our regulations for control should be based on observations in man, and in the case of vinyl chloride (VC) the concern is not only for angiosarcoma, but for other types of cancer as well. Health studies should be continued after the employee leaves the working force. At present there is no reason to suppose that there has been any measurable risk to the general public.

INDUSTRIAL HYGIENE

## &lt;64&gt;

Dowell, D.L., Handling vinyl chloride emergencies., Loss Prevention 5: 29-31 (1971).

A Manufacturing Chemists' Association CHEMTREC Program was developed in order to simplify reporting and receiving accident information involving vinyl chloride railroad tank cars, to aid in giving response to any caller regarding the immediate hazards of vinyl chloride monomer, and to aid in establishing liaison with both the accident scene and the shipper. Recommendations for handling vinyl chloride accidents in maritime transportation were also formulated. A burning tank car (200,000 lbs) of vinyl chloride, under unfavorable conditions of atmosphere and wind, will produce a ground level concentration of HCl of 5 ppm up to distances of 10,000 ft. As much as 20 to 30 ppm phosgene can be produced in the immediate vicinity of the fire, but the large quantities of HCl present will serve as a warning and a barrier, and the low levels of phosgene will be readily hydrolyzed and dissipated by the updraft of the flame. Combustion of vinyl chloride produces a very sooty flame with approximately 10% of the carbon converted to carbon black.

SAFETY; NON-OCCUPATIONAL EXPOSURE; DEGRADATION

## &lt;65&gt;

Drev, R.T.; Harper, C.; Gupta, B.W.; Talley, P.A., Effects of vinyl chloride exposures to rats pretreated with phenobarbital., Environ. Health Perspect. 11: 235-242 (1975).

Male rats pretreated with phenobarbital or a similar group treated with 3-methylcholanthrene were exposed to 13,500 ppm vinyl chloride (VC) 6 hrs/day for 10 consecutive days. Investigated were growth rate, organ weights, morphological changes, and both benzphetamine-N-demethylase activity and cytochrome P-450 content of liver microsomes. The only observed effect was a decrease in growth rate in the phenobarbital group, particularly apparent on the third day of VC exposure. Occasional morphological changes were also seen in the livers of these animals.

RAT; INTERACTION; PHARMACOLOGY; PHENOBARBITAL; METHYLCHOLANTHRENE

## &lt;66&gt;

Dublin, L.I.; Vane, R.J., Vinyl chloride, Occupation Hazards and Diagnostic Signs, Div. of Labor Standards, U.S. Dept. Labor Bull. No. 41: (Item 126) 64-65 (1941).

The acute toxicity of vinyl chloride was tested by the Bureau of Mines in single exposure experiments with guinea pigs and men. Unsteadiness, motor ataxia, incomplete and finally complete narcosis were produced in guinea pigs, with gross pathological findings of congestion and edema of the lungs, and hyperemia of the kidneys and liver. Men, exposed to 2.5% vinyl chloride for 3 min experienced dizziness and disorientation as to space and size, and complained of burning sensations in the soles of the feet. They recovered immediately when removed from the toxic fumes, and complained only of a slight headache which lasted 30 minutes.

TOXICITY; HUMAN; GUINEA PIG; NARCOSIS

## &lt;67&gt;

Dugois, P.; Amblard, P.; de Bignicourt, B.; Legrand, J., Acropathic polyvinylque professionnelle. (Occupational polyvinyl acroosteolysis.), Bull. Soc. Fr. Dermatol. Syphiligr. 79: 197-198 (1972).

A 34-year-old man who had worked for 2 years in a polyvinyl chloride plant was diagnosed as having edematous scleroderma of the hands and feet, edema of the face, and Raynaud's syndrome. Chemical treatment with steroids had little success, and the case was not followed after 6 months' treatment. Eleven years later, during a systematic examination, radiography of the hands showed characteristic aspects of occupational acroosteolysis with dissolution of the distal phalanges, which had not appeared in the earlier radiological examination.

Fr.

ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE; SKIN; CASE STUDY; BONE

## &lt;68&gt;

Environmental Protection Agency, Terre Haute vinyl chloride vapor escape., Smithsonian Institution Center for Short-lived Phenomena. Event Notification Report. Event 43-74, No. 1825 (1974).

On March 17, 1974, a railroad tank car carrying vinyl chloride overturned and was damaged, allowing vapors, but no liquid, to escape. Because vinyl chloride is an irritant and can affect the nervous systems, residents were evacuated from their homes for nearly 36 hours.

NON-OCCUPATIONAL EXPOSURE; HUMAN

## &lt;69&gt;

Environmental Protection Agency, Tentative method for the determination of vinyl chloride in the

<69> CONT.  
atmosphere (24-hour integrated sampling).  
Environmental Protection Agency, Methods  
Standardization and Performance Branch, Quality  
Assurance and Environmental Monitoring Laboratory  
Report, October (1974).

In a method applicable to measurement of vinyl chloride (VC) in ambient air using a 24-hr sampling period, VC is adsorbed on charcoal adsorbents which are subsequently extracted with carbon disulfide. The resulting solutions are measured chromatographically, using a flame ionization detector. Limit of detection is 0.001 µg/m<sup>3</sup> (1ppb). The maximum of the range is 20 µg/m<sup>3</sup> (8 ppm) which may be increased by extending the calibration range or by diluting the sample. Certain volatile hydrocarbons and freons have elution characteristics similar to VC, but no known common pollutants in ambient atmosphere at sufficient concentration cause interference. (This method has received no laboratory evaluation, and is still under investigation.)

#### ANALYSIS

<70>  
Environmental Protection Agency Task Force,  
Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride: A report on the activities and findings of the vinyl chloride task force., Environmental Protection Agency, Washington, D.C. 1-29 (Sept. 1974).

The Environmental Protection Agency is concerned 1) with the air emissions from vinyl chloride (VC) and polyvinyl chloride (PVC)--estimated by the Task Force to be 200 million pounds VC and 50 million pounds PVC discharged into the environment annually; 2) with aerosol sprays--a 30-second release could result in 400 ppm concentration in the air which will persist for several hours (aerosols are now banned); 3) accidental releases, as in transportation--16 rail accidents involving tank cars of VC were reported in the last three years; 4) VC trapped in water effluents, sludge, and other solid wastes, with particular concern for its appearance in drinking water; 5) the fate of unreacted VC monomer in the manufacture of PVC--ranging from as high as 8,000 ppm in the resin to as low as 5 ppm in finished PVC products; and 6) the migration of the monomer into water from PVC pipes and liners used in water systems. The Vinyl Chloride Task Force makes the following recommendations to and for the EPA in order to a) help clarify and reduce risks associated with VC and PVC, and b) take advantage of experiences with these chemicals in addressing other chemicals: 1) Establish air standards. Determine the possible ambient levels and the health risks associated with such levels. 2) Support regulatory actions under the Clean Air Act with additional ambient air monitoring, and correlate the measurements with specific in-plant activities. 3) Conduct detailed material balance studies in cooperation with industry, and correlate the magnitude and timing of estimated losses with monitored levels of VC. 4) Determine background levels of VC in both indoor and outdoor ambient air. 5) Monitor drinking water supplies which might be contaminated from VC discharges from nearby PVC plants. 6) Determine the amount of VC migrating from PVC products used in water distribution systems. 7) Standardize methods for monitoring levels of VC, and investigate the feasibility of developing continuous air monitoring devices. 8) Determine types and quantities of toxic substances leached or discharged from a) semi-solid and solid wastes generated by VC/PVC facilities, or b) PVC wastes discarded by consumers. Develop guidelines for control of storage and disposal of wastes, if studies indicate a hazard in this area. 9) Support currently planned VC toxicological studies. 10) Support currently planned VC epidemiological studies. 11) Industry and Government should support intensive studies on the behavior of VC in the atmosphere and in the environment, and particularly on its degradation

products and related chemical reactions. 12) Expand the Effluent Guidelines for the Plastics Industry promulgated under the Federal Water Pollution Control Act to cover the compounding and associated activities which result in discharges of toxic metals and other chemicals into the water. 13) Continue enforcement efforts to insure that pesticidal sprays containing VC as a propellant are removed from the channels of trade. 14) Keep regional, state, and local authorities informed of Agency efforts and encourage supportive action. 15) Build on VC experience for use with other chemicals. Make information on handling of VC available for assistance in responding to accidents resulting in release of VC. 16) Develop safe handling procedures for VC in the laboratory, and extrapolate these procedures to other carcinogens which may be of concern to the Agency. 17) Should the Toxic Substances Control Act be enacted, consider a) requirements for industrial testing of the toxicity of VC at low ambient levels and the persistence of VC in different media, and b) limitations on the levels of unreacted VC monomer in selected PVC products. 18) Continue leadership of Federal interagency activities with regard to VC and PVC, and develop an interagency mechanism to address problems associated with the plastics industry. 19) Stimulate government and industrial efforts to analyze in depth other high volume chemicals to identify those which need testing or controls to reduce potential environmental problems. Recommended Steps for Industry: 1) Improve operating and maintenance procedure in VC, PVC polymerization, and PVC fabrication facilities in order to reduce VC and PVC losses. Expand research and development efforts to develop new approaches to reduce losses. 2) Provide up-to-date information on character and extent of chemical pollutants which leave the plant as air, water, or solid waste discharges of degradation products. Operate systematic monitoring programs when essential. 3) Ascertain levels of unreacted VC monomer in all grades of PVC resin and advise purchasers accordingly. 4) Reevaluate, in consultation with interested Government agencies, the Manufacturing Chemists Association planned VC toxicological experiments at low doses to insure that they are statistically reliable and relevant to the ambient air concerns of EPA. Sectional headings to the report include: executive summary, character and scope of problems beyond the workplace, interests and activities of government agencies and industries, and recommendations.

#### STANDARDS; OCCUPATIONAL EXPOSURE; NON-OCCUPATIONAL EXPOSURE

<71>  
Environmental Protection Agency Task Force (A),  
Appendix I. Selected economical considerations.  
Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride., Report on the Activities and Findings of the Vinyl Chloride Task Force I: 1-5 (1974).

The U.S. vinyl chloride/polyvinyl chloride (VC/PVC) industry has operated for 40 years and shown an average annual growth of 14% over the past five years. During 1973, 5.3 billion pounds of VC and 4.6 billion pounds of PVC were produced, amounting to about 1/3 the western world's supply, with the U.S. consuming about 1/3 of the total. In 1973, 3.7% of PVC and 7.8% of VC produced in the U.S. were exported. Fifteen U.S. plants synthesize the monomer, 43 facilities polymerize PVC and copolymers, and at least 7,500 plants are engaged in fabrication of PVC products. About 1,500 workers are employed in monomer synthesis, 5,000 in polymerization, and an estimated 350,000 in fabrication plants. Should requirements for worker safety or environmental controls drive the price of PVC products up, many will probably be replaced by other plastics or disappear from the market. The major market categories of PVC products with their production levels, possible substitutes, and comparative price ranges are tabulated. Higher U.S. prices may stimulate increased imports. Several approaches to control of emissions are possible, but in many respects must be tailored to the individual

<71> CONT.

plants. Development of continuous flow processes, the use of larger kettles, better housekeeping, and/or reductions in the number of feed lines could dramatically reduce VC leakage.

#### ECONOMICS; ENVIRONMENT; PRODUCTION; STATISTICS

<72>

Environmental Protection Agency Task Force (B), Appendix II. Producers of vinyl chloride and polyvinyl chloride. Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride. Report on the Activities and Findings of the Vinyl Chloride Task Force II: 6-9 (1974).

Vinyl chloride producers, polyvinyl chloride producers, and polyvinyl chloride copolymer producers are tabulated, together with their locations and annual capacity in millions of pounds.

#### ECONOMICS; PRODUCTION; ENVIRONMENT

<73>

Environmental Protection Agency Task Force (C), Appendix III. The materials balance at vinyl chloride and polyvinyl chloride facilities. Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride. Report on the Activities and Findings of the Vinyl Chloride Task Force III: 10-16 (1974).

The production of vinyl chloride (VC) from ethylene and chlorine is diagrammed. It is difficult to estimate the areas and quantities of VC losses which come primarily from vent streams, the storage and transportation loading systems, and seepages from pumps. Total losses from a plant producing 500 million pounds of VC per year could amount to 500,000 pounds or approximately 0.1%. Some vented VC is converted to water and HCl; methane is flared; the heavy chlorinated hydrocarbons may be sold to solvent scrap dealers, dumped at sea, put into landfills or deep wells, or incinerated. The purity of the ethylene and chlorine fed into the units influences the by-products produced. More reliable data are available for estimating losses at polyvinyl chloride facilities, but each plant has its own idiosyncrasies. Older and smaller plants, with smaller reactors requiring more batch operations and changeovers from one type of resin to another, tend to have larger losses. Newer plants with multiple production lines allowing the dedication of one line to a given product result in lower resin loss due to product change. A properly run plant should be capable of a 95% yield. Present estimates put losses of VC at polymerization plants from 3.0 to 6.3%, while PVC losses are about 1.3%. Feed rate, reactor size, reactor cleaning procedures, batch sizes, and level of technology all influence the loss rate, but overall sloppy operation and the recovery system are the two most important factors.

#### ECONOMICS; ENVIRONMENT

<74>

Environmental Protection Agency Task Force (D), Appendix IV. Interim method for sampling and analysis of vinyl chloride in waste water effluents and air emissions. Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride. Report on the Activities and Findings of the Vinyl Chloride Task Force IV: 17-25 (1974).

This method for vinyl chloride (VC) determinations in water effluents, sludges and scums, and atmospheric emissions was developed during the monitoring program carried out by EPA in the spring of 1974, and was later refined. Water composite samples, air continuous composite bag samples, and air and water grab samples are analyzed without cleanup by gas chromatography (GC). Separations are effected by selection of one of two types of columns

depending upon the nature of the sample. Detection is by means of the flame ionization detector. Tetrahydrofuran extracts of sludges and scums are used for injection into the GC. Air continuous samples on activated carbon are extracted with carbon disulfide, and the extract is analyzed by direct injection into the GC. Calibration curves are developed using gravimetrically prepared calibration solutions, or by using known dilutions of VC in carrier gas. VC confirmation should be made by mass spectroscopic analysis of the GC eluent if possible. Independent confirmation may also be made in the event of extraordinarily high VC concentration samples by using long path Fourier transform IR spectrophotometry. This IR technique requires special equipment and about 20 cubic feet of air samples. Detailed are apparatus, materials, and procedures.

#### ANALYSIS; ENVIRONMENT

<75>

Environmental Protection Agency Task Force (E), Appendix V. Summary of regional activities. Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride. Report on the Activities and Findings of the Vinyl Chloride Task Force V: 26-30 (1974).

This Appendix briefly summarizes the vinyl chloride (VC) monitoring activities conducted at the following EPA Regional Offices during the spring of 1974. Region 1: Leominster, MA, Borden Chemical Co. (PVC); Region 2: Flemington, NJ, Tenneco Chemicals, Inc. (PVC); Region 3: Delaware City, DE, Stauffer Chemical Co. (PVC); Diamond Shamrock Chemical Co. (PVC); S. Charleston, WV, Union Carbide Corp. (PVC); Region 4: Louisville, KY, B.F. Goodrich Chemical Co. (PVC); Region 5: Painesville, OH, Nitroloy, Inc. (PVC); Robintech, Inc. (PVC); Region 6: Plaquemine, LA, Goodyear Tire and Rubber Co. (PVC); Dow Chemical Co. (VC); Region 9: Long Beach, CA, B.F. Goodrich Chemical Co. (PVC); American Chemical Corp. (VC); and American Chemical Corp. (PVC). Sampling and analyses were carried out in a short period of time using new methods based on previous analytical studies in which similar chemicals were evaluated. The nature of the polyvinyl chloride (PVC) manufacturing process results in the escape of VC pulses which lead to widely fluctuating levels of VC in the ambient air, and changes in air movement may influence concentrations at any given station. Therefore, the data reported are subject to change as additional monitoring is performed. Maximum emissions reported in the overall testing were: Water effluent: 22 ppm; Ambient air: 33 ppm; Sludge: 4200 ppm. Minimum emissions were in all cases below the detectable limit.

#### ANALYSIS; ENVIRONMENT; OCCUPATIONAL EXPOSURE; NON-OCCUPATIONAL EXPOSURE

<76>

Environmental Protection Agency Task Force (F), Appendix VI. Persistence of vinyl chloride. Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride. Report on the Activities and Findings of the Vinyl Chloride Task Force VI: 31-33 (1974).

The peak absorption of vinyl chloride (VC) in the ultraviolet region is below 2900 Angstroms, indicating that VC would not react in sunlight in the absence of other reactive chemicals. Laboratory results using simulated solar radiation in the presence of nitrogen oxides indicate a rate of reaction for VC of 8 to 10% per hour. Direct and indirect reaction products include ozone, nitrogen dioxide, carbon monoxide, formaldehyde, formic acid, and formal chloride. The low reaction rate of VC indicates that VC emissions will persist for a few miles downwind and can be considered a stable pollutant. Temperature inversions and lack of sunlight may cause a buildup of VC in the atmosphere. Reaction products are of concern in large industrial areas on sunny days. In water,

<76> CONT.

vinyl chloride is volatilized, rather than hydrolyzed, with the rate of loss depending on the rate of agitation or aeration. Photolysis does not appear to be of importance. With poor mixing in lakes or ponds and a continuous release of VC from sediments and sludges, it is conceivable that VC could persist long enough to accumulate biologically or cause other ecological effects. Up to 380 ppm VC were collected one minute after a 30 second release of insect spray in a small room.

NON-OCCUPATIONAL EXPOSURE; ANALYSIS; WATER; AEROSOLS; ENVIRONMENT

<77>

Environmental Protection Agency Task Force (G), Appendix VII. Health effects of VC. Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride., Report on the Activities and Findings of the Vinyl Chloride Task Force VII: 34-62 (1974).

Fifteen occupational cases of confirmed angiosarcoma of the liver have been discovered in the United States. Two are still alive and undergoing treatment. All were at one time "pot cleaners" where the potential for exposure to high levels of vinyl chloride (VC) was particularly great. The latent period for occupational angiosarcoma appears to be approximately 20 years. Ten cases of worker-related angiosarcoma of the liver have been reported from 5 foreign countries. Epidemiological data collected from the Connecticut Tumor Registry reveal three cases, one of whom worked in a PVC factory as an accountant, whereas the other two lived near polyvinyl chloride products plants. The significance of these cases must be further clarified. The Standardized Mortality Ratio (SMR) expresses the ratio of the number of deaths which actually occurred as a percentage of the number which would have been expected in a comparable population observed over the same age and time intervals. These ratios are tabulated from a mortality study of VC/PVC workers by Tabershaw/Cooper Associates. Data from 16 toxicological and epidemiological studies on vinyl chloride are also tabulated.

CANCER; ANGIOSARCOMA; HUMAN; CASE STUDY; TOXICITY; EPIDEMIOLOGY; POLYCHLORIDE

<78>

Environmental Protection Agency Task Force (H), Appendix VIII. Disposal of products containing polyvinyl chloride. Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride., Report on the Activities and Findings of the Vinyl Chloride Task Force VIII: 63-66 (1974).

The only large scale methods for disposal of solid wastes of polyvinyl chloride (PVC) are incineration and landfilling. Approximately 32,000 tons of PVC are burned annually, releasing about 18,500 tons hydrogen chloride (HCl) per year, the major toxic material in the air emissions. PVC is responsible for about 42% of the HCl released during the incineration of all municipal wastes in the United States. Other pollutants can also be formed during incineration, but it is highly unlikely that large quantities of vinyl chloride (VC) will be released. There is no evidence that PVC will revert chemically to VC. Technology exists for controlling the HCl emissions, but the process is expensive because of corrosion problems. PVC comprises about 0.2% of municipal solid waste in landfilling. It decomposes very slowly. Plasticizers are the additives of greatest concern with regard to leaching or gases. Separation of plastic waste from other municipal waste is a deterrent to recycling. Some types of PVC are being recycled in the manufacturing process.

NON-OCCUPATIONAL EXPOSURE; ENVIRONMENT; TOXICITY

<79>

Environmental Protection Agency Task Force (I), Appendix IX. Activities of Task Force. Preliminary assessment of the environmental problems associated with vinyl chloride and polyvinyl chloride., Report on the Activities and Findings of the Vinyl Chloride Task Force IX: 67 (1974).

The principal activities undertaken or stimulated by the Task Force from its inception in March, 1974, through July, 1974, are enumerated in chronological order.

ENVIRONMENT; EPA CHRONOLOGY

<80>

Fairhall, L.T., Vinyl chloride., Industrial Toxicology, 2nd ed., Hafner Publishing Co., New York Pt. 2: 356-357 (1969).

Vinyl chloride (VC), chloroethylene,  $CH_2=CHCl$ , is a colorless gas which condenses below  $-13.9^\circ C$ , freezes at  $-159.7^\circ C$ , boils at  $-13.9^\circ C$ , has a density 0.912/20 of 0.9121, and a vapor pressure of 2,300 millimeters of mercury at  $20^\circ C$ . VC limits of inflammability are 4.0 to 21.7 per cent by volume of air. VC is prepared by the chlorination of ethylene followed by the elimination of hydrogen chloride, accomplished industrially by passing the vapor of ethylene dichloride over such contact catalysts as alumina, activated charcoal, or pumice at high temperatures. VC polymerizes on exposure to sunlight and in the presence of peroxides or catalysts. Polymers are strong and resistant to water, and are used as rubber substitutes, coatings, insulation, films, foils, glass substitutes, refrigerants. Symptoms of exposure to the monomer are chiefly those of narcosis. VC does not diffuse a warning odor, but a 5% concentration gives a physiologic warning by producing symptoms of dizziness and disorientation in advance of harmful effects. No method has been developed specifically for determination of low concentrations of vinyl chloride as an aerial contaminant.

REVIEW; PROPERTIES; USES; OCCUPATIONAL EXPOSURE; HUMAN; NEUROLOGICAL

<81>

Falk, H.; Creech, J.L.; Heath, C.W., Jr.; Johnson, M.M.; Key, M.M., Hepatic disease among workers at a vinyl chloride polymerization plant., JAMA 230(1): 59-63 (1974).

To date, (Oct. 1974) 11 cases of hepatic disease, including seven cases of hepatic angiosarcoma, have been identified among employees at the Louisville, KY, vinyl chloride polymerization plant. All 11, white men, had worked at some time as reactor cleaners, the point of greatest exposure to vinyl chloride. Until the late 1960s, cleaning of the reactors was done manually, but since then high-pressure water hoses have been used because of the danger of acroosteolysis, a disease peculiar to polyvinyl chloride workers but not found in any of the angiosarcoma cases. All 11 had worked in close and continuous contact with the vinyl chloride polymerization process. Average work duration was 23.5 years for the five patients who spent nine months or less as reactor cleaners, and 15.1 years for the six men who spent 20 months or more as reactor cleaners, thereby suggesting a possible relationship between intensity of exposure and latent period for liver disease. Ages at diagnosis ranged from 28 to 58 years; duration of employment from 5 to 29 years. Pathologic review of specimens suggests a close similarity in the portal fibrosis, sinusoidal dilation, and atypical sinusoidal lining cells of the malignant and non-malignant cases. Conceivably such conditions represent a pre-malignant state which may be reversible if the worker is removed from the high-risk area.

LIVER; ANGIOSARCOMA; CANCER; OCCUPATIONAL EXPOSURE; EPIDEMIOLOGY; CASE STUDY

<82>  
 Pilatova, V.S., (Sanitary-hygienic conditions of work in the production of polyvinyl resins and measures of improvement.), Gig. Sanit. 22(1): 38-42 (1957).

Analysis of vinyl chloride (VC) in the air of a polyvinyl chloride (PVC) manufacturing plant was carried out by the method of Gronsberg, that is, photobromination of a solution of VC in chloroform with a solution of bromine in a mixture of chloroform and glacial acetic acid. VC concentrations fluctuated considerably but averaged 0.05 to 0.8 ag/l. Incidences of toxic angioneuroses among the workmen necessitated lowering the maximum allowable concentration of VC below the current legal limit of 1 ag/l.

Russ.; Eng. Summ.

STANDARDS; OCCUPATIONAL EXPOSURE; ANGIONEUROSIS

<83>  
 Pilatova, V.S.; Antonyuzhenko, V.A., (Changes in hygienic conditions of work and occupational disease-incidence among workers engaged in the production of polyvinyl chloride over a period of years.), Gig. Tr. Prof. Zabol. 15(4): 32-34 (1971).

Over a period of 16 years (1953-1968) air pollution by vinyl chloride within work premises of the polyvinyl chloride industry has been correlated with the incidence of occupational disease. Improvement of machinery, equipment, and ventilation have improved hygienic conditions in the premises. The clinical picture, accordingly, shows longer periods of exposure before development of disease. Considerable variability exists in clinical manifestations of chronic vinyl chloride poisoning as a function of environmental air contamination.

Russ.; Eng. Summ.

RAYNAUD'S PHENOMENON; SKIN; BONE; NEUROLOGICAL; CARDIOVASCULAR; OCCUPATIONAL EXPOSURE; EPIDEMIOLOGY

<84>  
 Pilatova, V.S.; Balakhonova, L.I.; Gronsberg, E.Sh., Hygienic conditions in the production of vinyl chloride., Gig. Tr. Prof. Zabol. 2: 6-9 (1958).

For an estimation of the degree of contamination in the work space air in a vinyl chloride production plant, about 300 samples of air were analyzed for maximum, minimum, and median content of chloroethane, methanol, and vinyl chloride. Improvement was directed toward the elimination of leakage and spills, insulation of portions of the production, and increased effectiveness in the ventilation arrangement of the work space.

Russ.

OCCUPATIONAL EXPOSURE; INDUSTRIAL HYGIENE

<85>  
 Pilatova, V.S.; Gronsberg, E.Sh.; Radzyukovich, T.M.; Reznik, M.D.; Tosichev, A.I., (Hygienic assessment of working conditions and health status of workers in the production of block polyvinylchloride.), Gig. Tr. Prof. Zabol. 18(1): 3-6 (1974).

Air pollution in the polyvinyl chloride (PVC) industry from vinyl chloride and PVC dust is caused by the intermittent nature of the technological process, reactor cleaning, imperfect sealing of apparatus, and noise from the machinery. These unfavorable conditions correlate with functional disorders in some workers. Remedial measures are recommended.

Russ.; Eng. Summ.

OCCUPATIONAL EXPOSURE; RAYNAUD'S PHENOMENON; SKIN; CARDIOVASCULAR; NOISE

<86>  
 Pilatova, V.S.; Gronsberg, E.Sh.; Smirnova, N.A.; Stulova, E.A.; Oreshkevich, L.V., (Industrial hygiene and the state of health in workers engaged in the production of polyvinyl chloride latex.), Gig. Tr. Prof. Zabol. 9(8): 9-14 (1965). (C167: 1036A3)

Individual sections of the polyvinyl chloride production line are pervaded with polyvinyl chloride dust and the work premises are polluted with vinyl chloride. Some operators handling vinyl chloride show changes in health conditions which are characteristic of initial forms of chronic poisoning. Health measures are recommended.

Russ.

OCCUPATIONAL EXPOSURE; INDUSTRIAL HYGIENE

<87>  
 Pilatova, V.S.; Vinogradova, V.K.; Bashkircova, L.S., (Hygienic evaluation of work conditions in some branches of chemical industry operating in the open air.), Gig. Tr. Prof. Zabol. 17(8): 8-11 (1973).

New ammonia and vinyl chloride plants should be built with key technological equipment outside in the open. Sanitation and hygienic conditions of work at existing open-air plants are quite satisfactory. A comparison of air pollution in a conventional factory and an open-air installation is made.

Russ.; Eng. Summ.

HUMAN; OCCUPATIONAL EXPOSURE; EQUIPMENT

<88>  
 Pilov, V.A., (Thermodynamic activity of volatile organic compounds and their action on mammals.), Biofizika 7(1): 73-79 (1962).

The thermodynamic activity of 84 substances, including vinyl chloride, was investigated in mice and rabbits relative to non-specific biological effects. Resultantly, thermodynamic parameters could be utilized only for an approximate classification of substances according to their type of action. The total number of carbon atoms in a compound, along with the logarithmic function of its activity, could however be used for the prediction of biological activity of corresponding concentrations of members of a homologous series. A similar relationship is effective for hypothesizing a comparative mechanism of the activity for the specific members of the homologous series.

Russ.

MICE; RABBIT; NARCOSIS; THERMODYNAMICS

<89>  
 Pine, S.D., Vinyl chloride as an ingredient of drug and cosmetic aerosol products., Fed. Register 39(166): 30830 (Aug. 26, 1974).

Effective September 25, 1974, any aerosol drug product containing vinyl chloride was declared to be a new drug, and hence a new drug application approved under section 505 of the Federal Food, Drug, and Cosmetic Act is required for marketing. A completed and signed "Notice of Claimed Investigational Exemption for a New Drug" is required to cover clinical investigations as evidence that such preparations are safe and effective for purposes intended. Any cosmetic aerosol product containing vinyl chloride is deemed to be adulterated under section 601(a) of the same act, and is subject to regulatory action.

REGULATION; AEROSOLS

R&S 135412

<90>

Fishbein, G.W., Publisher, Prof. Maltoni uses vinyl chloride to produce angiosarcoma by gastric route., Occupational Health and Safety Letter 5(6): 1 (1975).

On March 12, 1975 the National Institute for Occupational Safety and Health (NIOSH) was informed that, in Italy, Cesare Maltoni had produced angiosarcoma in rats by gastric intubation of vinyl chloride (VC) in olive oil. Angiosarcoma of the thymus developed in one rat after 45 weeks of feeding, and another animal developed angiosarcoma of the liver after 50 weeks. Additional details are forthcoming.

RAT; ANGIOSARCOMA; LIVER; THYMUS; INGESTION

<91>

Flinn, F.B., Industrial exposures to chlorinated hydrocarbons., Amer. J. Med. 1: 388-394 (1946).

This report reviews the toxicity of several industrial chlorinated hydrocarbons -- carbon tetrachloride, trichloroethylene, chloroprene, dichloromethane, chlorinated naphthalenes, and (only briefly) vinyl chloride. Vinyl chloride (VC) reacts somewhat like dichloromethane. VC is reportedly slightly toxic, is narcotic, and causes mild incoordination and ataxia as well as increased reaction time. Because of this induction of lethargy, VC may cause accidents to occur when the concentration is not high enough to cause noticeable narcosis.

OCCUPATIONAL EXPOSURE; PROPERTIES; TOXICITY

<92>

Gabor, S.; Lecca-Radu, M.; Manta, I., (Certain biochemical indexes of the blood in workers exposed to toxic substances (benzene, chlorobenzene, vinyl chloride).), Proa. Toksikol. i Klinika Prof. Zaboi. Khim. Etiol. 221-223 (1962). (CA 61: 11232a)

Liver function and oxidative processes were studied in 82 workers chronically exposed to vapors of benzene, chlorobenzene, and vinyl chloride. A decrease in catalase activity and increase in peroxidase and indophenoloxidase activity, and an increase in glutathione level in the blood were observed after 1 year of exposure to vinyl chloride. Such a study is recommended for diagnosis of early changes in liver function.

Russ.

DIAGNOSTIC; LIVER; HUMAN; OCCUPATIONAL EXPOSURE

<93>

Garcia Perez, Jose, La polimerizacion del Cloruro de Vinilo y sus riesgos. (The polymerization of vinyl chloride and its hazards.), Ion Rev. Esp. Quim. Appl. 29: 376-377 (1969).

Some of the European literature concerning the polymerization of vinyl chloride and the resultant potential hazards to health are reviewed. No references.

Span.

REVIEW

<94>

Gay, B.W.; Lonnesan, W.A.; Bridbord, K.; Moran, J.B., Measurements of vinyl chloride from aerosol sprays., Ann. N.Y. Acad. Sci. 246: 286-295 (1975).

Five experiments designed to determine human exposure levels and decay of vinyl chloride were performed in home and office environments which simulated normal everyday use of the aerosol sprays. In all cases, the user is exposed to high peak concentrations, even with good ventilation in the room. The decrease in vinyl chloride concentration with time appears to be a dilution effect of room

ventilation. An approximated relation of predicted general population exposures from aerosols to an occupational exposure situation reveals that on a time-weighted average basis, the exposure could be well above the current proposed occupational standard.

AEROSOLS; NON-OCCUPATIONAL EXPOSURE; STANDARDS

<95>

Gedigk, P.; Mueller, R.; Sechtelsheimer, H., Morphology of liver damage among polyvinyl chloride production workers. A report on 51 cases., Ann. N.Y. Acad. Sci. 246: 278-285 (1975).

Histological findings from 51 cases of liver disease were classified into five groups: 1) degenerative changes of liver parenchyma, 2) adaptive responses were occasionally manifest as a ground-glass appearance of the cytoplasm, attributed to an adaptive increase of the smooth endoplasmic reticulum, 3) fibrosis was found in two forms -- fibrosis of the portal tracts and septa, and an intralobular, perisinusoidal, net-like fibrosis with collagenization of sinusoid walls, 4) hepatocytes were hyperplastic with evidence of proliferative activity, and 5) sinusoidal cells were activated and showed marked proliferative activity, with hyperchromatic and polymorphic nuclei which were obviously an expression of polyploidy. Together with the pattern of the degenerative lesions, this proliferation of sinusoidal cells may be considered rather characteristic of vinyl chloride damage. There is an obvious relationship between the total time of exposure and the changes of the sinusoidal cells. The proliferation and, particularly, the polymorphism and hyperchromasia of the nuclei clearly increase in proportion to exposure time.

PATHOLOGY; HISTOLOGY; LIVER

<96>

Gibney, L., Toxic Substances Control Act. Could it prevent the vinyl chlorides of tomorrow?, Chem. Eng. News 53(11): 12-13 (1975).

A House of Representatives' version of last year's Toxic Substances Control Act is expected in April. Hearings are being held (March, 1974) on the Senate version, S. 776. Major provisions of the Senate version are: 1) The Environmental Protection Agency (EPA) administrator is required to prescribe standards for test protocols for chemicals. 2) Manufacturers must notify the EPA administrator of plans to manufacture or import new chemicals 90 days before beginning commercial production. 3) The administrator can approve sale and distribution or either halt or restrict manufacture and distribution of a chemical except for export. 4) Manufacturers or citizens may challenge the action of the administrator through suit in U.S. District Court. 5) Manufacturers are required to submit safety and health data from studies in progress as well as those made since 1935. 6) The director of EPA's Office of Toxic Substances is to be a Presidential appointment and must be qualified in the chemicals and health field. 7) The bill authorizes \$11 million for the fiscal year ending June, 1976, and \$12.6 million to fiscal year ending Sept. 1977.

REGULATION; MANUFACTURE

<97>

Gilbert, S.G., Low molecular weight components of polymers used in packaging., Environ. Health Perspect. 11: 47-52 (1975).

Chronic toxicity of migrating residues and additives from polymers used in the packaging of foods and drugs is of importance in the increasing use of such polymers. To develop useable and practical safety standards one must consider the origin and chemical nature of potential migrants, the methods of transfer, and the basic underlying principles of safety.

<97> CONT.  
STANDARDS; HUMAN; NON-OCCUPATIONAL EXPOSURE

<98>  
Gitsios, C.T., Acro-osteolysis in PVC workers., *Med. Bull.* (Standard Oil Co., NJ), 31(1-3): 49-56 (1971).

The manufacture of polyvinyl chloride (PVC) and some literature relating to diseases of PVC polycleaners is reviewed briefly. Esso polycleaners hand-scraped the reactors only after the concentration of vinyl chloride monomer reached 50 ppm or less. The Esso Pappas PVC plant is described in the illustrated article which details the industrial hygiene measures and program of medical check-ups to be followed by employees of the plant.

OCCUPATIONAL EXPOSURE; REVIEW; ACROOSTEOLYSIS;  
HUMAN; POLYCLEANER; RAYNAUD'S PHENOMENON;

<99>  
Goethe, R.; Callesan, C.J.; Ehrenberg, L.; Wachtmeister, C.A., Trapping with 3,4-dichlorobenzethiol of reactive metabolites formed in vitro from the carcinogen vinyl chloride., *Ambio* 3(6): 234-236 (1974).

In experiments to determine if chloroethylene oxide is formed as a reactive metabolite of vinyl chloride (VC) by epoxidation through microsomal detoxification enzymes, 3,4-dichlorobenzethiol was used as a trapping agent. An air-vinyl chloride mixture was passed through the supernatant of a rat liver homogenate freed from nuclei, mitochondria, and other particles by centrifugation. The supernatant was fortified with all necessary cofactors for a mixed function oxygenase system, and also with 3,4-dichlorobenzethiol. After 2 hours of exposure to the VC gas, the mixture was extracted with hexane, and the fractions were analyzed by gas chromatography-mass spectrometry. 3,4-Dichlorophenylthioacetaldehyde was identified by its mass spectrum, isotope distribution pattern, and base peak. A second peak with molecular weight of 248, apparently formed directly from vinyl chloride and the thiol, was not identified. In another experiment designed to trap only the volatile metabolites of vinyl chloride, by eliminating the thiol from the liver homogenate and passing the VC gas mixture through a second tube containing 3,4-dichlorobenzethiol dissolved in methanol, the same two products were found. The results are in accordance with the formations of chloroethylene oxide and/or chloroacetaldehyde as in vitro metabolites of vinyl chloride.

BIOCHEMISTRY; METABOLISM

<100>  
Grigorescu, I.; Toba, J., Vinyl chloride: Industrial toxicologic aspects., *Rev. Chim. (Bucharest)* 17(8): 499-501 (1966). (CA66: 1239p).

Vinyl chloride may react with water at the level of the hepatic cell, yielding ethylene monochlorohydrin, which may subsequently oxidize to chloral and chloroacetic acid. An analytic method using paper chromatography and colorimetry was developed for detection of chloroacetic acid in the urine. None was detected in the urine of healthy personnel, but 80% of the staff who had been employed 2-5 years in a vinyl chloride processing plant gave positive results. In these cases, the alpha-globulin fraction of protein was higher and the gamma-globulin fraction was lower than in persons with presumably no chloroacetic acid in the urine. Thus capacity to metabolize chloroacetic acid seemingly decreased after 2 years of chronic insult.

Non.

HUMAN; BIOCHEMISTRY; DIAGNOSTIC; OCCUPATIONAL EXPOSURE

<101>  
Gronsborg, E.Sh., Colorimetric determination of vinyl chloride in air., *Khim. Pros.* 42(7): 510-511 (1966). (CA 65: 17592a)

Air is drawn through tubes containing activated carbon, and the loaded carbon is then treated with a 1:1 mixture of acetic acid and ethyl alcohol. After 10 min. an aqueous mixture of potassium persulfate and iodic acid is added and the mixture is shaken. It is then decolorized with 30% sodium sulfite and centrifuged. A chromotropic acid solution is added and the mixture heated in a boiling water bath, cooled, and diluted. The color is measured at 574 millimicrons, or compared with standards. Ethylene is an interference.

ANALYSIS

<102>  
Gronsborg, E.Sh., Determination of vinyl chloride in the air., *Gig. Sanit.* 11: 43-44 (1954).

This method is based on bromination of VC using a solution of bromine in a 1:1 mixture of chloroform and glacial acetic acid. Sensitivity of the determination equals 0.10 µg VC per sample. VC is absorbed from the air, at the rate of 10-12 l/hr during passage across chloroform cooled to 10-15 degrees. Ethylene and chlorine do not present interference.

Russ.

ANALYSIS

<103>  
Hamilton, A.; Hardy, H.L., *Plastics. Vinyl polymers and copolymers.*, Industrial Toxicology. Publishing Sciences Group, Inc., Acton, MA 3rd ed., 340-344 (1974).

Polyvinyl chloride (PVC) is a thermoplastic which can be reheated and reshaped repeatedly. The finished PVC has been found to be without injurious properties, but the monomer, vinyl chloride (VC), has recently become suspect as a potent carcinogen since the report of several cases of hepatic angiosarcoma in a single VC polymerization plant. Thermal degradation products of PVC include the monomer and hydrochloric acid fumes. Dizziness and confusion are caused by VC. It is implicated in acroosteolysis, a disease occurring in men who clean PVC polymerization vessels by hand, although the actual toxic agent and its mechanism of attack is unknown. One process for the production of vinyl chloride uses mercuric chloride as a catalyst, and has been responsible for the introduction of mercury into natural waters, where it enters the food chain.

MERCURY; ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON;  
POLYCLEANER

<104>  
Hardie, D.W.F., Vinyl chloride., *Kirk-Othmer Encyclopedia of Chemical Technology* 2nd ed., 5: 171-177 (1964).

An extensive patent bibliography is included in this review of industrial processes, physical and chemical properties, economic aspects, technical standards, handling and toxicity, and uses of vinyl chloride (VC). VC may be stored or transported under pressure, and may have stabilizers added. Bulk transportation is in tank trucks, with transfer to storage vessels by pumping or blowing, sometimes under a nitrogen atmosphere. Leakages must be detected by means of soap solution, never a halide lamp, because of the flammability and explosibility of VC. VC exerts a narcotic action like that of ethyl chloride as well as being similar in toxicity. VC causes dizziness and disorientation at 5% by volume, and at 20 to 40% it is rapidly fatal to small test animals. Concentration in work spaces should not exceed 500 ppm, at which there is no evidence of direct injury from prolonged exposure.

R&S 135414

<104> CONT.  
PROPERTIES; PATENT; MANUFACTURE; USES; TOXICITY

<105>  
Harris, D.K., Health problems in the manufacture and use of plastics., Brit. J. Ind. Med. 10: 255-268 (1953).

A survey of the most common synthetic plastics and associated materials is reported. Examples of addition polymers and condensation polymers, with certain additives, are presented with relative clinical and pathological effects. Second-degree burns received by accidental spraying with vinyl chloride comprise a case study. Initial sensations resembled local anesthesia. The condition healed within two weeks.

SKIN; HUMAN; CASE STUDY; INDUSTRIAL HYGIENE

<106>  
Harris, D.K.; Adams, W.G.P., Acro-osteolysis occurring in men engaged in the polymerization of vinyl chloride., Brit. Med. J. (3): 712-714 (1967).

Two male autoclave cleaners engaged in the manufacture of polyvinyl chloride displayed acroosteolysis in fingers and sacroiliac joints. Also, the patella was affected in one case, whereas in the other the phalanges of the feet were involved. Raynaud's phenomenon and skin lesions accompanied the condition. One man had cleaned autoclaves since 1950, the other since 1960. Mechanical methods of cleaning these autoclaves should be adopted.

ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON; HUMAN; CASE STUDY; BONE; SKIN; EPIDEMIOLOGY; OCCUPATIONAL EXPOSURE

<107>  
Heath, C.W., Jr.; Falk, H.; Creech, J.L., Characteristics of cases of angiosarcoma of the liver among vinyl chloride workers in the United States., Ann. N.Y. Acad. Sci. 246: 231-236 (1975).

Epidemiologic features of vinyl chloride (VC) indicate that either prolonged exposure and/or a long interval from initial exposure is required before liver disease becomes apparent. Nonalignant diseases of the liver, as well as incidence, clinical aspects, and epidemiology of angiosarcoma, were included in this study. Manifestations of liver disease are quite variable, and detection was sometimes difficult until hepatic fibrosis was so far advanced that splenomegaly and increased portal pressure were evident. A major concern is to develop a sensitive means for detecting liver disease in the early stages.

EPIDEMIOLOGY; DIAGNOSTIC

<108>  
Heath, C.W., Jr.; Key, M.M., Nationwide surveillance of angiosarcoma of the liver., Arch. Environ. Health 29: 360 (1974).

In the Center for Disease Control, the National Institute of Occupational Safety and Health and the Bureau of Epidemiology have established a surveillance registry for cases of angiosarcoma of the liver in the U.S. in response to the recent discovery that some cases may stem from exposure to vinyl chloride. Physicians in contact with such cases are urged to contact the Center for Disease Control, Bldg. 1, Room 520, Atlanta, GA 30333. The national surveillance registry is part of the epidemiologic study underway to define the apparent relationship between hepatic angiosarcoma and exposure to vinyl chloride. Full participation by physicians is solicited.

EPIDEMIOLOGY; LIVER; ANGIOSARCOMA; HUMAN; LETTER

<109>  
Heck, V.W.; Pires, E.G., Growth of plants fumigated with saturated and unsaturated hydrocarbon gases and their derivatives., Texas Agr. Expt. Sta. MP-603 12 pages (1962).

Squash, cotton, corn, soybean, and cowpeas were fumigated with 10, 100, and 1,000 ppa of acetylene, ethylene, ethylene oxide, propylene, and vinyl chloride. Plant height, leaf size, flower bud number, cotyledon injury, and an overall injury index were criteria for effects. Ethylene oxide appears to be a true toxicant. Symptomatology of ethylene, acetylene, propylene, and vinyl chloride injuries were identical suggesting a common metabolic pattern producing a physiological response. With the exception of ethylene, concentrations of these gases would reach injurious-to-plant levels only in very exceptional circumstances, and are not important as air pollutants. Vinyl chloride was the least injurious in a relative analysis of all five gases.

AGRICULTURE; TOXICITY; PLANTS

<110>  
Hefner, R.E., Jr.; Watanabe, P.G.; Gehring, P.J., Preliminary studies of the fate of inhaled vinyl chloride monomer (VCM) in rats., Environ. Health Perspect. 11: 85-95 (1975).

Rats, exposed to initial concentrations of vinyl chloride monomer (VCM) ranging from 50 to 1167 ppa, metabolized the gas via a primary pathway, postulated to involve alcohol dehydrogenase for levels below 220 ppa. In rats exposed to concentrations at and exceeding this level, the primary pathway saturates, and metabolism occurs via a secondary pathway(s), postulated to be epoxidation and/or peroxidation. For all concentrations disappearance followed apparent first order kinetics. Unrelated to dose, rat liver sulphydryl content (glutathione and cysteine) is reduced following exposure to 50-15,000 ppa VCM. The primary metabolites of VCM seemingly react with the nonprotein sulphydryl. The degree of reduction is reduced with repeated daily exposure. Metabolites excreted in the urine appear to be S-(2-hydroxyethyl)cysteine and S-(2-carboxymethyl)cysteine and the N-acetyl derivatives. Monochloroacetic acid may also be a metabolite.

BIOCHEMISTRY; RAT; METABOLISM; LIVER

<111>  
Hefner, R.E., Jr.; Watanabe, P.G.; Gehring, P.J., Preliminary studies of the fate of inhaled vinyl chloride monomer in rats., Ann. N.Y. Acad. Sci. 246: 135-148 (1975).

Rats exposed to concentrations of vinyl chloride (VC) below 100 ppa metabolize it in  $t_{1/2} = 86$  min but in concentrations exceeding 220 ppa,  $t_{1/2} = 261$  min indicating that the predominant pathway is saturable. Pyrazole inhibits the metabolism of VC suggesting metabolism via alcohol dehydrogenase. Inhibition of metabolism of VC by ethanol was less pronounced at concentrations of 1000 ppa than at 100 ppa, suggesting that metabolism occurs via pathways other than alcohol dehydrogenase at the higher concentrations. Metabolism via microsomal oxidases is suggested by the depression of metabolism by SKF 525-A in rats exposed to over 1,000 ppa VC, with no effect at levels of 65 ppa. Monochloroacetic acid was found in urine of rats exposed to 5000 ppa VC daily for 9 weeks. VC exposure reduces the nonprotein sulphydryl concentration of the liver, with a tendency for the reduction to become less pronounced with repeated daily exposures. Ethanol reduces this depression of concentration of nonprotein sulphydryl in rats exposed to 1000 ppa VC. In rats exposed to 89 ppa, VC is metabolized to polar products which appear to be derived after initial metabolism of VC and subsequent conjugation with glutathione and/or cysteine through covalent binding with the sulphydryl. These metabolites are

## &lt;111&gt; CONT.

excreted in the urine, a small fraction is metabolized to CO<sub>2</sub> and expired, and another small fraction appears to be retained in the liver and other tissues for as long as 75 hrs. Hypotheses based on these observations are discussed.

## METABOLISM; RAT

## &lt;112&gt;

Reisann, H.; Lillis, P.; Hawkins, D.T., A bibliography on the toxicology of vinyl chloride and polyvinyl chloride., Ann. N.Y. Acad. Sci. 246: 322-337 (1975).

This bibliography of 389 references is listed alphabetically by first author, together with sequential numbering. The bibliography is subdivided by subject matter into the following categories with pertinent references indicated by number in each category: Carcinogenesis, Effects at cellular level discussed, Carcinoma, Mesangiosarcoma, Vinyl chloride disease, Liver, Liver cirrhosis, Portal hypertension, Lung effects, Skin effects, Acroosteolysis, General experimental, Thorotrast, Arsenic, Nitrosamines, Polyvinyl chloride, Measurement and control, Industrial processes, Plastics.

## BIBLIOGRAPHY

## &lt;113&gt;

Hess, E.V.; Schneider, H.; Roush, G., Clinical studies in occupational acroosteolysis--a new disease., J. Lab. Clin. Med. 70(6): 1023 (1967).

Twenty male workers underwent a comprehensive clinical investigation to detect involvement of the hematologic, immunologic, metabolic, hepatic, renal, cardiac, and pulmonary systems, which might be attributed to association with vinyl chloride polymerization processes. Fifteen men had Raynaud's phenomena, of whom 7 had temperature changes on provocative testing, 11 had skin changes with fibrotic-like lesions on hands and forearms, and 9 had pseudoclubbing. Ten men had definite and 6 had equivocal neurotropic-like changes in the hands, and 4 were normal. Two had delayed emptying of the esophagus; none showed x-ray lung changes. Varying degrees of dermal sclerosis were shown in 11 skin biopsies. Some or all of these lesions, including bone changes, are reversible.

ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON; SKIN; BONE; LUNG; CASE STUDY

## &lt;114&gt;

Miraiwa, K., Effect of narcotics upon the flexion reflex of rat., Osaka Daigaku Igaku Zasshi 5(1): 95-100 (1952). (BA 28: 11025)

Disappearance of the flexion reflex in the hind limb of the intact rat was studied under narcotics. The flexion reflex curve showed that the latency of response to a single electrical stimulation was 12 to 15 milliseconds and the peaks of contraction appeared at 30 to 60, 60 to 80, 100, 150, 250 milliseconds, etc. The group of narcotics which included vinyl chloride did not change the latency period, but the peaks at 250 to 400 milliseconds disappeared, and after 400 milliseconds other peaks appeared.

Jap.; Eng. Sum.

NARCOSIS; NEUROLOGICAL; RAT

## &lt;115&gt;

Holmberg, B.; Holma, G., The industrial toxicology of vinyl chloride. A review., Work-environ.-hth 11: 138-144 (1974).

This review with 49 references summarizes the pertinent literature on vinyl chloride (VC) toxicity in man and animals. Technically, the most widely

used synthesis of VC is by oxychlorination of ethylene. The monomer is used as propellants for deodorants, pesticides, hair sprays, and furniture polish, but its main use is as resin for plastic production. Threshold limit values at the end of 1973 were 100 ppm in West Germany, 10 ppm in the Soviet Union, 500 ppm in Sweden and 200 ppm in the United States. Standards were lowered to a time-weighted average of 1 ppm and a ceiling value of 5 ppm for 15 minutes in the USA and Sweden as of January 1, 1975. Acute and chronic toxicity with symptoms of acroosteolysis, Raynaud's phenomenon, liver function abnormalities, and liver cancer are discussed from an epidemiological standpoint. Toxicological data from animal studies indicate that VC is a multipotential carcinogen in animals and perhaps in man.

REVIEW; CANCER; ACROOSTEOLYSIS; EPIDEMIOLOGY; HUMAN; RAT; MICE; INDUSTRIAL HYGIENE

## &lt;116&gt;

Monna, M. (Ed.); Crosby, H.J. (Ed.), Symposium on toxicity in the closed ecological system., Defense Documentation Center for Scientific and Technical Information AD440942, pp 9-18 (1963).

In a compilation of all contaminants identified in the atmosphere of a Mercury spacecraft, the concentration of vinyl chloride was recorded as 0 to 3 ppm. Exposures in spacecraft are unalleviated and continuous for 24 hr/day, 7 day/week. New criteria of safety are needed.

STANDARDS; SPACECRAFT

## &lt;117&gt;

Mori, M.; Kobayashi, Y.; Ota, Y., Vinyl chloride monomer odor concentration., Plast. Ind. News 18(11): 164-168 (1972).

Vinyl chloride, a colorless gas at normal temperature and pressure, produces narcotic symptoms at 1,000 ppm. Though emitting an odor similar to chloroform, the threshold of detection may vary 10 times between subjects, and further depends on the subjects' acclimatization to the odor. Vinyl chloride monomer was diluted with air and supplied slowly in increasing concentration to the nostrils of 5-10 workers selected at random from each of 15 polyvinyl chloride manufacturing plants. The stench perceptive concentration, a ratio between the concentration of gas and the perception point, was thus determined. Sixty percent of the workers perceived the monomer at 500 ppm; 1,000 ppm was necessary for perception by all workers. Concentration of the gas below the perceptive concentration was studied by a gas detection tube and gas chromatography.

SAFETY; OCCUPATIONAL EXPOSURE

## &lt;118&gt;

Infante, P.F., Oncogenic and mutagenic risks in communities with polyvinyl chloride production facilities., Conference on Occupational Carcinogenesis. New York Academy of Sciences, New York, N.Y. (March 24-27, 1975). (Abstract) Ann. N.Y. Acad. Sci. (To be published)

A significantly greater number of children with malformations were born during the period 1970-73 in the three Ohio communities with polyvinyl chloride production facilities, when compared with the expected malformation statistics for the entire state. The rate of malformations in the index cities was significantly greater than in the counties in which these cities were located. Comparable county-city combinations did not reveal the same differences. Most notable anomalies were those involving the central nervous system: 17 observed vs 5.62 expected among live births; 8 vs 2.85 among stillbirths. In 2 communities a significant excess of deaths from CNS tumors in adult males 45 years of age and older was observed. These preliminary findings indicate the need for

<118> CONT.  
further study of possible contributing factors.

MUTAGENICITY; TERATOGENICITY; CARCINOGENICITY

<119>  
Izserov, M.F., (The toxic action of vinyl chloride.), Tech. Pub. Branch, Information Services Div., EPA Tr. 9-75: 1-10 (1974).

The development of chronic occupational intoxication by vinyl chloride was first established by investigators of the Gorky Institute of Occupational Hygiene and Disease in 1950. Observations of 183 persons over a 27-year period at the Institute show that the angioneuroses and acroosteolysis are only part of the clinical picture of intoxication caused by the injury principally to the nervous system. Mild acute intoxication proceeds with a prearctic syndrome (mild agitation, euphoria, nausea, disturbance of coordination, somnolence). Symptoms vanish in fresh air. Symptoms of chronic intoxication appear in a significant number of workers within a 3-months to 5-year exposure period. Initial manifestations are Raynaud's syndrome and acroosteolysis. Later, in addition to neurological disturbances, the liver is enlarged in 1/3 of all cases, with some functional disturbance of protein metabolism. There is a tendency toward anemia with mild hemolytic phenomena. Gaye-Vernike type brainstem encephalopathy may develop with increasing anisocoria, gross eye-motor disturbances, insufficiency of facial and sublingual nerves with mask-like face, and gross deviation of the tongue. Hallucinations, paroxysmal disturbances of consciousness, and dysphoric episodes may appear. Hypertension, cardiovascular insufficiency, and dystrophic changes in the myocardium develop in a significant number of patients. Peripheral blood shows a tendency toward erythrocytosis and enlarged forms of erythrocytes. Changes in the esophagus and gastro-intestinal tract are manifested by difficulty in swallowing, choking, fullness in the stomach. Acidity of the stomach contents is reduced. Structural disturbances in the brainstem section of the brain account for most of the observed disturbances of internal organs and disorders of vascular regulation. Despite the long period of observation on a large number of patients, no cases of hemangiosarcoma of the liver were observed.

Russ.; Eng. Transl.

OCCUPATIONAL EXPOSURE; RAYNAUD'S PHENOMENON;  
NEUROLOGICAL; GASTROINTESTINAL; CARDIOVASCULAR;  
BLOOD; HEMAN; LIVER; ACROOSTEOLYSIS; ANGIONEUROSIS;  
REVIEW

<120>  
Jackson, H.L.; McCormack, W.B.; Rondestvedt, C.S.; Saelitz, K.C.; Viele, I.E., Safety in the chemical laboratory LIX. Control of peroxidizable compounds., J. Chem. Educ. 47: 175-188 (1970).

Structure, detection, and examples of compounds which are potential peroxide formers are discussed with emphasis on suggested procedures for handling and storage. Vinyl chloride is hazardous due to peroxide initiation of polymerization; storage recommendations include a yellow label and insuring less than 12 months shelf storage.

EXPLOSIVE; SAFETY; PEROXIDE

<121>  
Jaeger, R.J., Vinyl chloride monomer: Comments on its hepatotoxicity and interaction with 1,1-dichloroethylene., Ann. N.Y. Acad. Sci. 286: 150-151 (1975).

A similarity is noted between vinyl chloride (VC) and vinylidene chloride (1,1-DCE) although 1,1-DCE is the more reactive and a potent hepatotoxin. Workers at B.F. Goodrich in Louisville who developed angiosarcoma of the liver were exposed to both

compounds. Atmospheric concentrations of VC up to 4.65% (v/v) produced no elevation of serum alanine-alpha-ketoglutarate transaminase (AKT) in 4-hr exposures to fasted rats. Chronic exposure to VC caused reduction in rat liver glutathione concentrations. VC prevented 1,1-DCE injury in fasted rats by an undetermined mechanism. Monochloroacetic acid as a urinary metabolite suggests formation of ethylene chlorohydrin as an intermediate. Intramolecular nucleophilic displacement of chlorine by the hydroxyl group on the alpha carbon results in a positively charged protonated epoxide which fulfills the criteria for electrophilicity of alkylating groups as a requirement for tumorigenicity. This hypothesis of tumorigenicity should be tested; other monohaloethenes may be more tumorigenic than vinyl chloride. (preliminary data)

CARCINOGENICITY; LIVER; 1,1-DICHLOROETHYLENE

<122>  
Jaeger, R.J.; Conolly, R.B.; Murphy, S.D., Short-term inhalation toxicity of halogenated hydrocarbons. Effects on fasting rats., Arch. Environ. Health 30: 26-31 (1975).

Vinyl chloride monomer (VC) was not hepatotoxic to fed rats or rats fasted for 18 hours, following 4 hr exposures of 10,522 and 46,554 ppm. To test the synergism or antagonism of VC with 1,1-dichloroethylene (DCE), the two were administered simultaneously to fed and fasted rats, and serum alanine-alpha-ketoglutarate transaminase (AKT) activity determined. VC was not toxic at 1,122 ppm in fasted rats, whereas DCE produced injury at 205 ppm. The combined exposure of 1,056 ppm VC to 195 ppm DCE (a molar ratio of 5 to 1) resulted in complete protection of fasted rats. Injury occurred in 2 of 5 fasted rats at an equimolar concentration. Simultaneous exposure of fasted rats to 12,093 ppm VC and 1,971 ppm DCE did not increase either serum AKT or serum dehydrogenase sorbitol (SDH). Vinyl chloride was therefore antagonistic to the hepatotoxic effect of DCE.

RAT; LIVER; FASTING; INTERACTION; DICHLOROETHYLENE

<123>  
Jaeger, R.J.; Conolly, R.B.; Reynolds, E.S.; Murphy, S.D., Biochemical toxicology of unsaturated halogenated monomers., Environ. Health Perspect. 11: 121-128 (1975).

Inhalation toxicity studies show that 1,1-dichloroethylene, 1,1-dibromoethylene, and 2-chloro-1,3-butadiene are more toxic to fasted rats than to fed rats. Vinyl chloride monomer and 1,1-difluoroethylene were not acutely hepatotoxic at 46,500 and 82,000 ppm respectively in normal male rats whether fed or fasted.

TOXICITY; RAT

<124>  
Jaeger, R.J.; Reynolds, E.S.; Conolly, R.B.; Moslen, M.T.; Szabo, S.; Murphy, S.D., Acute hepatic injury by vinyl chloride in rats pretreated with phenobarbital., Nature 252(5485): 724-725 (1974).

Exposure to 5% vinyl chloride monomer (VCM) for 6 hrs in an inhalation chamber caused acute liver injury to rats pretreated for 7 days with phenobarbital (PBT). Injury was assessed at 24 hr by serum enzyme assays (alanine-alpha-ketoglutarate transaminase and sorbitol dehydrogenase) and histology examination after perfusion fixation revealed vacuolization of centrilobular parenchymal cells and focal necrosis of mid-zonal parenchyma. A ten-fold decrease in exposure concentration to 0.5% VCM for 6 hr caused no apparent injury to either PBT pretreated or non-pretreated rats. Only after nonpretreated rats were exposed to 10% VCM (an anesthetic dose) for 6 hr did a slight elevation of serum enzymes and centrilobular vacuolization occur. Activation of VCM to an epoxide intermediate might

<124> CONT.  
occur by a mechanism similar to that proposed for trichloroethylene.

RAT; PATHOLOGY; INTERACTION; PHARMACOLOGY;  
PHENOBARBITAL

<125>  
Jaeger, W.J.; Reynolds, E.S.; Szabo, S.; Moslen, M.T.; Murphy, S.D., Inhalation toxicity studies of vinyl chloride monomer in phenobarbital or Aroclor 1254-pretreated rats., Abstracts of Papers for 18th Annual Meeting of Society of Toxicology, Williamsburg, Virginia, March 9-13 (1975) Abstract No. 27: p. 23 (1975).

Exposure to 60,000 ppm vinyl chloride (VC) led to an approximate 50-fold increase of serum alanine-alpha-ketoglutarate transaminase (SALT) in 7-day phenobarbital (PB)-treated fasted rats, while PB-treated fed rats only exhibited increased enzyme activity approximately 7-fold. SALT was elevated after exposure of PB-treated rats to 40,000 ppm VC, but no fed-fasted difference was apparent. Also, 20,000 and 5,000 ppm VC showed no elevation in SALT. Fasted rats, treated for 7 days with Aroclor 1254, had elevated SALT after exposure to 25,000 ppm VC. Rats treated with 100,000 ppm VC alone for 6 hrs showed no elevation of SALT.

INTERACTION; TOXICITY; RAT; PHENOBARBITAL; AROCLOR 1254

<126>  
Jensen, S.; Jernelov, A.; Lange, R.; Palsork, K.R., Chlorinated by-products from vinyl chloride production: A new source of marine pollution., Marine Pollution and Sea Life. M. Ruivo, Ed., Fishery Resources Division, FAO, Fishing News (Books), Ltd., Surrey, Eng. 24-244 (1970).

Chlorinated aliphatic hydrocarbon (C-Cl) by-products of vinyl chloride production were sampled in the North Atlantic from June to September 1970; toxicity tests were performed using algae, cod, plaice, crustaceans, molluscs, and echinoderms. Cod and plaice proved most sensitive; thirteen ppm caused a 50% reduction in photosynthesis. Chemical analysis by chromatography showed that C-Cl originates from industries on both sides of the Atlantic and is widely distributed. Degradation experiments showed that the various C-Cl components disappeared at varying rates; in water with no biological activity however, C-Cl remained unchanged up to 27 days at room temperature.

TOXICITY; BY-PRODUCTS; MARINE

<127>  
Johnson, C.A., Clinical management of workers exposed to vinyl chloride and polyvinyl chloride., Ann. N.Y. Acad. Sci. 286: 313-319 (1975).

The medical surveillance program at the Goodyear plant in Niagara Falls consists of the following: 1) a comprehensive medical history, 2) physical examination, 3) anterior and posterior x-rays of the chest, 4) x-ray of both hands, 5) pulmonary function test, and 6) extensive clinical laboratory testing program. Effective clinical management must include, in addition to the medical surveillance, the cooperation of the toxicologist, the process engineer, the industrial hygienist, the physician, and the worker.

OCCUPATIONAL EXPOSURE; DIAGNOSTIC

<128>  
Jeehe, S.; Lange, C.-E., Sklerodermaartige Hautveränderungen, Raynaud-Syndrom und Akroosteolysen bei Arbeitern der PVC-herstellenden Industrie. (Scleroderma-like skin alterations, Raynaud's syndrome, and acroosteolysis in workers in the polyvinyl chloride industry.), Deut. Med. Wochenschr. 97: 1922-1923 (1972).

Cold sensitivity, irritation, numbness, blanching, and pain of the fingers were reported by seven patients over a period of 1 to 3 1/2 years. Later, a drumstick-like enlargement of the ends of the fingers and an hourglass shaping of the nails occurred. Clinical diagnosis confirmed 5 cases of Raynaud's syndrome. Knobby ivory-colored infiltrates were observed in finger joints, backs of the hands, and underarm areas while three patients exhibited a thickened, fleshy, mask-like appearance in the upper cheek area. Band-forming osteolysis was seen in five patients. Disturbances of liver and respiratory function occurred in two patients. Differentiation of vinyl chloride effects from scleroderma is possible by 1) the relative frequency in comparison to scleroderma, 2) exclusively an illness of men, 3) lack of important early symptoms as shortening of tongue ligaments and sclerosis of the esophagus, 4) swelling and shortening of finger end phalanges, and 5) acroosteolysis, seldom seen in scleroderma.

Ger.

ACROOSTEOLYSIS; BONE; SKIN; RAYNAUD'S PHENOMENON; LIVER; LUNG; HUMAN; OCCUPATIONAL EXPOSURE; POLYCLONAL

<129>  
Jeehe, S.; Lange, C.-E.; Stein, G.; Veltan, G., Ueber die sog. Vinylchlorid-Krankheit (eine neue Berufskrankheit), (The so-called vinyl chloride illness, a new occupational illness.), Berufsdermatosen 22: 4-22 (1974).

Lesions of skin, bones, vascular and hematopoietic systems, liver, spleen, and lungs suggest a systemic disease caused by prolonged exposure to vinyl chloride in autoclave-workers in the polyvinyl chloride industry. The connective tissues undergo an unknown alteration together with development of fibrosis of the skin and of the vascular system, and perhaps of the lungs and liver as well. The authors suggest renaming the syndrome called "occupational acroosteolysis" to the more inclusive term "vinyl chloride disease."

Ger.; Eng. Sum.

LIVER; SKIN; BONE; LUNG; ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE; CASE STUDY

<130>  
Jeehe, S.; Lange, C.-E.; Stein, G.; Veltan, G., Ueber die sogenannte Vinylchlorid-Krankheit. (The so-called vinyl chloride illness.), Deut. Med. Wochenschr. 98: 2034-2037 (1973).

Thirteen workers aged 29 to 50 yrs (avg 39 yrs) with an employment span from 2 to 18 yrs (avg 7 yrs) in a polyvinyl chloride manufacturing plant were examined. First symptoms appeared in 11 patients between 1 1/2 to 3 1/2 yrs exposure to the monomer. In 2 patients symptoms appeared at 7 and 11 years exposure. Initial symptoms included cold sensitivity and numbness or crippling in hands and feet; thickening of finger-ends and loosening of the nails; and general complaints such as fatigue, slowing of responses, forgetfulness, dizziness and nausea at work, sweating, upper abdominal discomfort, and skin changes. Principal findings on examination were: splenomegaly of either a primary toxic origin or a secondary effect; toxic liver damage ranging from slight histological alterations to hypertrophic cirrhosis in the portal area and intrahepatic block in advanced cases; restrictive alterations and partial insufficiency in the respiratory system perhaps due to the same alterations in collagen and elastic fibers seen in the skin; cardiovascular disturbances evidenced by Raynaud's phenomenon and cold sensitivity, thrombocytopenia, reticulocytosis, and leucopenia; changes in the esophagus; and changes in the skin and bones which led to band-forming osteolysis and fragmentation of the phalanges. The symptom complex is not a known syndrome, and etiology and

R&S 135418

<130> CONT.  
pathogenesis are still to be clarified. Vinyl chloride is implicated in a brief literature review.

Ger.

HUMAN: CASE STUDY; REVIEW; LUNG; LIVER;  
CARDIOVASCULAR; RESPIRATORY; BONE; SKIN;  
ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON

<131>  
Kallanovich, P.L., (Sanitary-chemical characteristics of polyvinyl-chloride floor coatings.), Gig. Sanit. (Hyg. Sanit.) 33(1-3): 274-280 (1968).

Air above polyvinyl chloride tiles and floor coverings was examined for vinyl chloride. Analyses for unsaturated hydrocarbons were performed at the same time as those for vinyl chloride. Neither hydrocarbons nor vinyl chloride were released after 30 days, but the liberation of toxic substances during the first 30 days was sufficient to require an intensive ventilation period of 1 1/2 to 2 months before use in children's institutions. Further toxicological investigations were recommended. The laboratory procedures are detailed.

Russ.; Eng. Transl.

SAFETY; DEPOLYMERIZATION; CHILD; HUMAN; STANDARDS;  
NON-OCCUPATIONAL EXPOSURE

<132>  
Replinger, M.L.; Goode, J.W.; Gordon, D.E.; Calandra, J.C., Interim results of exposure of rats, hamsters, and mice to vinyl chloride., Ann. N.Y. Acad. Sci. 246: 219-224 (1975).

An interim summary of tumors in mice exposed to vinyl chloride for 8 months in concentrations of 50 to 2500 ppm, showed tumors in lung, liver, and mammary glands, with metastases of the mammary tumors to the lung at all levels of exposure. No tumors have been observed in rats or hamsters exposed to 50 ppm, but angiosarcomas may have been observed in one male hamster and one male rat exposed to 2500 ppm, and in one female rat exposed to 200 ppm. These tentative data will be expanded as the study continues.

CARCINOGENICITY; RAT; MICE; HAMSTER

<133>  
Kern, W.H., vinyl chloride and liver tumors., JAMA 229(10): 1286 (1974).

This letter to the editor makes the distinction between primary carcinoma of mesodermal origin, a type of sarcoma, and primary carcinoma, a tumor of considerably greater frequency. The two types have been confused in certain comments on the literature.

LIVER; CANCER; DIAGNOSTIC

<134>  
Key, M.H., Occupational dermatitis from plastics., J. Med. Assoc. GA 57: 421-424 (1968).

Polymers cause little dermatitis. Most industrial dermatitis in the polymer field occurs in curing or hardening of thermosetting resins, and is caused by monomers, low molecular weight polymers, condensate components, or additives. The acute stage is manifested by erythema, edema, and vesicles, and is accompanied by pruritis. The chronic stage has a dry, scaly, fissured, and lichenified appearance and is also pruritic. Polyvinyls have caused little dermatitis, and until recently the polyvinyl manufacturing process was thought to be safe. Acroosteolysis was first reported in 1964 among polycleaners, and is thought to be caused by vinyl chloride monomer or by a peroxy-compound. The acroosteolysis is usually reversible if detected early.

ACROOSTEOLYSIS; POLICLEANER; DERMATITIS; SKIN

<135>

Key, M.H., NIOSH Recommended Standard for occupational exposure to vinyl chloride. (Excerpts from a March 11, 1974, memorandum.), National Institute for Occupational Safety and Health, U.S. Department of Health, Education, and Welfare U.S. Government Printing Office: 657-060/2007 (1974).

On January 22, 1974, B.F. Goodrich Chemical Co. informed NIOSH that several deaths may have been related to occupational exposures, particularly those in the area of vinyl chloride polymerization. On February 1, 1974, a briefing between NIOSH/CDC and other Federal agencies with health research responsibilities concluded that vinyl chloride was the prime etiological agent in causing angiosarcoma of the liver as an occupational disease. At an OSHA Informal Fact-Finding Hearing on Possible Hazards of Vinyl Chloride Manufacture and Use on February 15, 1974, some preliminary data were presented which showed induction of angiosarcoma of liver and other organs, as well as other cancers, in rats exposed to vinyl chloride. Consequently it is recommended that any employee exposed to measurable concentrations of vinyl chloride shall wear an air-supplied respirator. The employer is required to develop a Control Plan to reduce airborne concentrations of vinyl chloride to levels not detectable by the recommended method. The standard applies only to the manufacture of synthetic polymer from vinyl chloride. Regulated areas shall include loading operations; storage and transfer facilities; polymerization processes and operations; and resin handling, compounding, packaging, and storage areas. Routine operations shall include 1) Measurement of vinyl chloride in air at strategic sampling points under normal operating conditions, 2) Control Plan for controlling vinyl chloride levels and developing additional healthful work practices, 3) Periodic tests for leaks or emission of vinyl chloride, 4) Use of full-face, air-supplied respirator until exposure to vinyl chloride is reduced below detectable levels, 5) Specific and detailed transfer procedures for loading or transferring vinyl chloride monomer, 6) Full-body protective clothing in regulated areas, and 7) Impervious containers for disposal of protective clothing and equipment. Reactor and vessel entry procedures and techniques shall be developed to minimize employee exposure to vinyl chloride. Maintenance and decontamination activities are to be conducted to prevent airborne contamination and accidental skin contact. A roster of employees entering regulated areas shall be maintained for a period of 20 years. Emergency procedures, informative signs and labelling, and training requirements are established. Pre-employment and periodic health examinations directed primarily to detect liver disease and/or hepatic tumor shall include the following tests of liver function: a) total bilirubin, b) alkaline phosphatase, c) serum glutamic oxalacetic transaminase, d) serum glutamic pyruvic transaminase and e) gamma glutamyl transpeptidase. Regulated areas, number of employees in each regulated area, and a Control Plan shall be reported within 60 days to OSHA; results of air measurement samples shall be reported semi-annually; and all incidents which release vinyl chloride monomer to employee exposure shall be reported.

STANDARDS; OCCUPATIONAL EXPOSURE; HUMAN

<136>

Kovac, A.; Kurajica, L.; Juric-Ruzic, D.; Parac, B., Acropathia extremitatum in polymerisation vinylchloridi -- new occupational disease., Liječnicki Vjesnik (Med. J.) 91(1): 5-17 (1969).

Case studies of autoclave cleaners in a polyvinyl chloride (PVC) manufacturing plant led to the designation of the newly observed occupational disease as "Acropathia extremitatum in polymerisation vinylchloridi" to comprise all a

<136> CONT.

stages of the disease within the definition and emphasize the occupational origin. The stages are: 1) transient subjective Raynaud-type symptoms such as pallor and numbness, 2) changes in color and quality of skin, 3) combination of 1 and 2 with recent, shallow, marginal, bony lesions of terminal phalanges, 4) combination of 1, 2, and 3, with definitive bone changes, including permanent shortening and thickening of fingertips with applanation and transversal widening of nails. If the worker is removed from exposure, prognosis is relatively favorable with no marked decreases in working ability, although fingertips are permanently deformed with lessened tactile sensitivity.

ACROOSTEOLYSIS; CASE STUDY; OCCUPATIONAL EXPOSURE; BONE; SKIN

<137>

Krazer, C.G.; Mutchler, J.E., The correlation of clinical and environmental measurements for workers exposed to vinyl chloride., Amer. Ind. Hyg. Assoc. J. 33(1): 19-30 (1972).

A newly developed statistical technique correlates clinical manifestations with individual levels of environmental vinyl chloride exposure. A retrospective survey of 98 healthy male workers exposed chronically to vinyl chloride for periods up to 25 years indicates that vinyl chloride, together with smaller amounts of vinylidene chloride, causes certain physiological and clinical changes. The "step-wise multiple linear regression analysis" technique requires good environmental and medical data in substantial quantity for relating measured clinical changes directly to measured exposure. More studies are needed on worker populations exposed only to vinyl chloride.

REVIEW; STANDARDS; OCCUPATIONAL EXPOSURE; MODEL; CASE STUDY; EPIDEMIOLOGY

<138>

Krantz, J.C.; Carr, C.J.; Musser, R.; Harne, W.G., The effect of chlorinated ethylenes on the perfused leg vessels of the frog., Arch. Int. Pharmacodyn. 52: 369-372 (1935).

The vasoconstrictive action of ethylene, vinyl chloride, cis and trans dichloroethylene, trichloroethylene, and tetrachloroethylene was investigated by perfusing the vessels of frog's legs. Vinyl chloride was dissolved in Ringer's solution containing 5% methyl alcohol. A saturated solution of phosgene in a parallel experiment tested the effect of decomposition products of the chlorinated ethylenes; but no vasoconstrictive effect was found, nor could vinyl chloride be prepared in sufficient concentration to elicit a response.

NEUROLOGICAL; CARDIOVASCULAR

<139>

Kudryavtseva, O.P., (Characteristics of electrocardiographic changes in patients with vinyl chloride poisoning.), Gig. Tr. Prof. Zabol. 14(8): 54-56 (1970).

Together with the vasoneuroses in the clinical picture of chronic vinyl chloride intoxication, disturbances of the cardio-vascular system which appear on electrocardiographic examination occupy a significant place. Condition of the patient's heart can be followed and supervised by means of the electrocardiograph.

Russ.

HUMAN; CASE STUDY; CARDIOVASCULAR; ANGIONEUROSIS

<140>

Kuebler, H., The physiological properties of aerosol propellants., Aerosol Age 9(4): 44, 47-48, 50, 90-91

(1964).

Vapor pressure, boiling point, solubility, chemical resistance, flammability, and low toxicity are important in aerosol propellants. One hundred and twenty each of mice, rats, and guinea pigs, in groups of 10 (5 male, 5 female), were exposed 2 hrs/day for 100 days to an open inhalation system with constant air flow of 0.5, 1.5 and 5.0 vol % of several propellants, including vinyl chloride. Animals were fed a normal diet and weighed weekly. No effects from vinyl chloride were noted up to 1.5%; 5 vol % increased mobility and then reduced it as tests progressed. Effects were reversible. Growth, blood pattern, condition of the liver, and histopathology and morphology of internal organs were normal. One gram vinyl chloride yielded 39.5 mg CO, 0.11 mg phosgene, and 102 mg HCl at 1000 C in thermal decomposition tests. No skin reaction was observed in 500 tests with 50 patients using aerosol propellants, including vinyl chloride.

AEROSOLS; TOXICITY; DEGRADATION; RAT; MICE; HUMAN; GUINEA PIG

<141>

Kuebler, H., Vinyl chloride and methylene chloride., Perfum. Kosmet. 40(11): 625-627 (1959).

Seventy grams of vinyl chloride can be sprayed in a 50 cubic meter space before reaching the Maximum Acceptable Concentration of 500 ppm. Up to 100 times this amount, or 20 eighteen-ounce cans of spray will produce only a slight physiological effect. Narcosis begins at 12 vol % or the equivalent of 50 eighteen-ounce cans. Favorable properties of vinyl chloride for an aerosol medium include a pressure of 2 atmospheres at 20 degrees C, good solvent properties for lacquers and perfumes, lack of odor, high ignition temperature, dermatological inertness, and very low toxicity. Methylene blue or copper ion are effective as polymerization inhibitors in the spray cans.

Ger.

AEROSOLS; HUMAN; PROPERTIES; TOXICITY

<142>

Kuebler, H., Vinyl chloride as an aerosol propellant., Aerosol Age 3(9): 26, 28, 59-61 (1958).

An inhalation test of vinyl chloride (VC) performed on mice indicated that exposures to 0.5 and 5.0% by volume VC (2 times/day for 60 days for periods of 1/2 hr each) produced no observable changes in behavior, well-being, or appetite. No damage or bodily injury was observed on dissection at either concentration. Dermatological tests using an aerosol sun-tan oil pressurized with vinyl chloride applied over a 5 day period to ear-lobes and arm-pits of people aged 18 to 73 years showed no skin reactions. Maximum allowable concentration is quoted at 500-1000 ppm, and the safe experience of loaders and fillers of aerosol cans over a period of years is cited.

AEROSOLS; NON-OCCUPATIONAL EXPOSURE

<143>

Lange, C.-E.; Juebe, S.; Stein, G.; Veltman, G., Further results in polyvinyl chloride production workers., Ann. N.Y. Acad. Sci. 246: 18-21 (1975).

Fifteen workers in the polyvinyl chloride (PVC) processing industries (mixing and manipulation of basic PVC powder in processes where gases, fumes, and smoke tend to develop) were examined. Occupational exposure to PVC ranged from 1 1/2 yrs to 13 yrs with an avg of 5 yrs. Complaints included pressure and/or pain in the upper abdomen, dizziness, cold hands and feet, and leg weakness. Clinical symptoms included thrombocytopenia, increased BSP retention time, reticulocytosis, leukopenia, splenomegaly, and changes in the liver. Two recommendations are made: a) Mass examinations

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<143> CONT.

of PVC production workers be extended to PVC processing industries, b) Research on the liberation of vinyl chloride monomer during PVC processing be instituted. A second problem concerns the determination of a causal relationship between working in PVC production and the formation of lethal malignant tumors. Two case histories are presented, but no definitive connection is drawn.

OCCUPATIONAL EXPOSURE: SPLEEN; LIVER;  
THROMBOCYTOPENIA; LEUKOPENIA; RETICULOCYTOSIS;  
CANCER: HUMAN; CASE STUDY

<144>

Lange, C.-E.; Juehe, S.; Stein, G.; Veltman, G., Die sogenannte Vinylchlorid-Krankheit--eine berufshedingte Systemasklerose? (The so-called vinyl chloride sickness - an occupation-related systemic sclerosis?), Int. Arch. Arbeitsmed. 32: 1-32 (1974).

Out of 13 workers employed at a polyvinyl chloride factory for 1 3/4 to 14 years, 8 had scleroderma-like skin changes; 7 patients had thickened finger phalanges; 11 patients had circulatory disturbances; 4 had Raynaud's syndrome; and 6 had band-like osteolysis of the terminal finger phalanges. Thrombocytopenia was observed in all patients; 12 had splenomegaly; 11 had liver malfunction; 4 had esophageal varices; and 8 had pulmonary insufficiency. Long-term exposure to vinyl chloride vapors is suspected of causing these extensive pathologic changes. The suggested name for this systemic disease is "vinyl chloride disease".

Ger.; Eng. Summ.

OCCUPATIONAL EXPOSURE: SKIN; LUNG; LIVER; ESOPHAGUS;  
ACROOSTIPOLYSIS; RAYNAUD'S PHENOMENON;  
THROMBOCYTOPENIA; CARDIOVASCULAR; EPIDEMIOLOGY;  
OSTEOLYSIS

<145>

Lange, C.-E.; Juehe, S.; Veltman, G., Liver angiosarcoma in two workers in a PVC-producing factory., Deut. Med. Wochenschr. 99: 1598-1599 (1974).

Case studies describe two workers in a polyvinyl chloride manufacturing plant who died of angiosarcoma of the liver after 11 and 12 years exposure. In view of similar case histories from other countries and the results of animal research, the authors are lead to the assumption of an occupationally related cause.

Ger.; Eng. Summ.

ANGIOSARCOMA; LIVER; OCCUPATIONAL EXPOSURE; CASE STUDY

<146>

Lassiter, D.V., Case Study 3. Vinyl Chloride--best available technology., Conference on Occupational Carcinogenesis, New York Academy of Sciences, New York, N.Y. (March 24-27, 1975). (Abstract) Ann. N.Y. Acad. Sci. (To be published.)

The standard for vinyl chloride (VC) marked the first Federal attempt to regulate occupational exposure to a carcinogen on the basis of available analytical methodology. The importance of polyvinyl chloride (PVC) to the Nation's economy rendered zero exposure limits impractical. Exposure was therefore limited to 1 ppm on an 8-hr time-weighted-average and 5 ppm on a 15-minute time-weighted average, based on recommendations by the National Institute for Occupational Safety and Health, which represented the sensitivity of available analytical methodology for determination of compliance.

STANDARDS; ANALYSIS

<147>

Lavery, D.S.; Wilks, P.A., Vinyl chloride analysis by infrared spectroscopic methods., Amer. Lab. 6(10): 53-60 (1974).

Continuous industrial monitoring is required in work area surveys, in leak detection, and in potentially high-hazard areas. Infrared analyzers are compared with other types of detectors as to speed, sensitivity, stability, specificity, reliability, accuracy, portability, and maintenance requirements. Characteristics of infrared vinyl chloride analyzers, and infrared analytical data for vinyl chloride are presented. Experimental portable and fixed-installation infrared analyzers are described which are fail-safe and require little maintenance. Output from such monitors can be computerized for data storage, exposure calculations, and warnings of hazardous levels. Comparison of methods are tabulated for: flame ionization hydrocarbon analyzers, halide detectors, automated gas chromatographs, and selective wavelength (infrared) analyzers with long path cells.

ANALYSIS; OCCUPATIONAL EXPOSURE

<148>

Lee, P.I.; Marry, D.S., Angiosarcoma of the liver in a vinyl-chloride worker., Lancet 1(7870): 1316-1318 (1974).

A 71-year-old man, who had worked in the production of polyvinyl chloride from vinyl chloride monomer for 20 years, was admitted to emergency treatment with massive edema, moderate ascites, and a palpable liver. Liver scintiscan showed diffuse liver enlargement with patchy uptake, and liver-biopsy showed fragmentation, but normal architecture. There was no evidence of hepatoma or fibrosis, but a mild portal-tract infiltrate was noticed. The overall picture suggested cirrhosis. Two weeks later the patient died suddenly. The liver was composed of irregular interconnecting reddish-brown honeycombed areas of malignant hemangioendothelioma (angiosarcoma) separated by pale brown liver tissue of apparently normal structure. Adjacent tissue was infiltrated, but in areas away from the tumor, there was no evidence of cirrhosis. Angiosarcoma of the liver appears to be an occupational tumor with considerable variation in susceptibility; vinyl chloride is the suspected carcinogen.

CASE REPORT; REVIEW; LIVER; HUMAN; ANGIOSARCOMA;  
CASE STUDY

<149>

Lefaux, R., Vinyl Chloride., Practical Toxicology of Plastics. Chemical Rubber Co. Press, Cleveland, OH Pt. 2, Ch. 1, No. 7: 80-83 (1968).

Vinyl chloride (VC) -- CH<sub>2</sub>CHCl, monochloroethylene -- is at ordinary temperatures a colorless gas with a sweet, though not marked, odor. VC polymerizes very readily. Vapors form inflammable mixtures with air above -78 C; 4-22% volume in air is explosive. Flares are controllable with carbon dioxide. Animal experiments showed narcosis ranging from no signs in 480 min at 10,000 ppm to death in 10-20 min at 400,000 ppm. Over 500 ppm irritates the eyes. Physiological action is compared with ethyl chloride. At 1,000 ppm humans show slight anesthesia, drowsiness, slight visual disturbances, faltering gait, numbness, and tingling of extremities. VC is a primary skin and mucous irritant, and rapid evaporation can cause burns. Factory ventilation should allow no more than the maximum permitted concentration of 500 ppm or 1,300 mg/m<sup>3</sup> (Great Britain and USA, 30mg/m<sup>3</sup> in Russia). Exposure to higher concentrations necessitates use of safety goggles, gas mask, apron, and rubber gloves. Vinyl chloride is not corrosive when dry, but in the presence of moisture it attacks iron and steel. It can be transported and stored at room temperature under pressure.

Fr.; Eng. Transl.

<149> CONT.  
OCCUPATIONAL EXPOSURE; SAFETY; EXPLOSIVE; SKIN;  
NEUROLOGICAL; PROPERTIES; STANDARDS; REVIEW

<150>

Lehmann, K.B.; Flury, F., Monochloroethylene (Vinyl chloride), Toxicology and Hygiene of Industrial Solvents, Williams and Wilkins Co., Baltimore, Md. pp. 170-172 (1943).

Local irritation and general toxic effects from vinyl chloride (VC) are very slight. VC is suitable for supplementary narcosis because of low toxicity, wide range of effect, low concentration in the blood (15-17 eq% in narcosis), and rapid elimination (82% in 10 min). Heart and blood pressure are not affected, and there are no after-effects. Mice and rats had no liver or kidney injuries after 8 hrs exposure per day for 5-8 days. Dogs showed no liver or kidney damage after repeated exposures at 10 vol %, but at 20 vol % kidney respiratory paralysis, strong saliva flow, and vomiting occurred. Lethal concentration for narcosis in humans is 7-10 vol %; above 12% is dangerous. Death occurs due to respiratory paralysis with resultant heart arrest. Hyperemia of lung and kidneys, and pulmonary edema, but no serious pathological changes were found on dissection of test animals. Confusion, intoxication, headaches, burning of the soles of the feet, and other subjective disturbances occur in humans, but recovery is rapid.

Ger.; Eng. Transl.

TOXICITY; RAT; MICE; DOG; GUINEA PIG; HUMAN; NARCOSIS

<151>

Lester, D.; Greenberg, L.A.; Adams, W.R., Effects of single and repeated exposures of humans and rats to vinyl chloride, Amer. Ind. Hyg. Assoc. J. 24: 265-275 (1963).

Rats exposed to 5% vinyl chloride for up to two hours exhibited moderate intoxication; respiratory failure occurred at 15%. Rats exposed to 5% daily for 19 days or to 2% for 92 days showed increased spleen and liver weights, decreases in white cells, and an increase in red cells. No effects were observed on the lungs, growth rate, hemoglobin, hematocrit, or prothrombin time. Increase in liver weight was associated with morphological changes in the liver which appeared to have no pathological significance. No meaningful morphological alterations were evident in either kidneys or spleens. Based on these experimental results, the accepted threshold limit value of 500 ppm seems to offer an adequate margin of safety for human exposure.

STANDARDS; RAT; HUMAN; NON-OCCUPATIONAL EXPOSURE;  
LIVER; SPLEEN; KIDNEY; LUNG; BLOOD; OCCUPATIONAL  
EXPOSURE

<152>

Lillis, R.; Anderson, R.; Nicholson, W.J.; Dams, S.; Fischbein, A.S.; Selikoff, I.J., Prevalence of disease among vinyl chloride and polyvinyl chloride workers., Ann. N.Y. Acad. Sci. 246: 22-41 (1975).

More than half of 354 workers with vinyl chloride (VC) exposure ranging from less than 2 yrs to more than 20 yrs reported symptoms of acute preneoplastic effects. Prevalence of the following abnormalities increased with length of VC exposure: abnormal circulation in fingers and toes, cyanosis, sensitivity to cold, numbness and tingling of fingers, Raynaud's syndrome, and abnormal Allen test indicating delayed arterial circulation. Both total exposure and duration from onset of exposure were of importance in the likelihood of abnormality. Hepatosplenomegaly was found in 15% and splenomegaly in 3% of the workers. A correlation of 41% was found between the cases of hepatosplenomegaly and splenomegaly and a finding of elevated alkaline phosphatase. Thrombocytopenia was present in only one patient. The prevalence of lung changes increased with the

duration of exposure, and was correlated to some extent with peripheral circulation abnormalities. Evaluation of pulmonary changes requires further study of extraneous exposures. Future exposure to VC should be controlled in order to prevent development of adverse effects, including cancer.

OCCUPATIONAL EXPOSURE; LUNG; LIVER; CANCER;  
RAYNAUD'S PHENOMENON; CARDIOVASCULAR; EPIDEMIOLOGY

<153>

Nakk, L.; Creech, J.L.; Whelan, J.G.; Johnson, M.M., Liver damage and angiosarcoma in vinyl chloride workers. A systematic detection program., JAMA 230 (1): 64-68 (1974).

The first recognized human angiosarcomas of the liver associated with vinyl chloride monomer polymerization were discovered in Louisville, KY, when a physician noted diagnosis of the rare angiosarcoma on a death certificate and recalled doing a biopsy three years earlier which resulted in a similar diagnosis. Because both patients had worked in the production of polyvinyl chloride, a systematic detection program was devised whereby large numbers of workers could be screened for liver disease with relative ease. The initial laboratory procedure for detection was a 12- or 18-factor automated chemical analysis. The 12-factor analysis consisted of tests for the following: calcium, inorganic phosphorus, glucose, blood urea nitrogen (BUN), uric acid, cholesterol, total protein, albumin, total bilirubin, alkaline phosphatase, lactic acid dehydrogenase (LDH), and serum glutamic oxaloacetic transaminase (SGOT). The 18-factor analysis consisted of the preceding plus creatine phosphokinase (CPK), creatinine, and serum electrolyte determinations. If one liver abnormality was found, the 12-factor analysis was repeated in three weeks. If it persisted or if two or more liver-related abnormalities were found, a comprehensive examination was made consisting of tests for the following values: a 12-factor automated chemical analysis, serum electrophoresis, LDH isoenzymes, fractionated alkaline phosphatase, direct and indirect bilirubin (if total level was elevated), serum glutamic pyruvic transaminase (SGPT), G-glutamic transpeptidase (GGTP), isocitrate dehydrogenase (ICD), A-fetoprotein (fetoglobulin), and carcinoembryonic antigen (CEA). Also, a complete blood cell count (CBC), platelet count, chest roentgenogram, and liver and spleen scan were done. If serious liver disease were possible, hepatic panangiography, consisting of hepatosplenic arteriograms and phlebograms with free and wedged hepatic pressure measurements were made. If a tumor was suggested, open-liver biopsy, with hepatic lobectomy if so indicated, was advised. Clinical and roentgenographic studies were also made. In the context of this condition, when roentgenographic studies indicated cirrhosis, histopathologic examination often revealed a peculiar portal fibrosis and Kupffer cell hyperplasia. Such a surveillance program helps to detect liver damage in an early, possibly reversible or curable state, but even borderline abnormalities must be carefully followed up.

HUMAN; ANGIOSARCOMA; CANCER; LIVER; DIAGNOSTIC

<154>

Maltoni, C., Occupational carcinogenesis., International Congress Series No. 322 (ISBN 90-219-0228-1) Cancer Detection and Prevention, Proceedings of the 2nd International Symposium on Cancer Detection and Prevention, Bologna, Italy, April 9-12 (1973) 19-26 (1973).

The frequency of occupational cancer has increased with industrialization; risks must be evaluated by epidemiology or by experimental testing--results are often considered equivalent. Any agent producing tumors in animals is potentially carcinogenic for man. Inhalation apparatus for controlled dosage was built and carcinogenic bioassays of vinyl chloride (VC) using rats produced thyroid gland carcinoma, nephroblastoma, angiosarcoma, and cancers of other

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types. Various chemical agents suspected of being carcinogenic are listed and frequency of cellular atypias in several chemical industries are charted. Methods of prevention include experimental testing of all new agents; up-to-date epidemiological data; legal outlawing of production and utilization of strong carcinogens; technical protection in production of weak or suspected carcinogens; medical checks of all workers.

#### CARCINOGENICITY; OCCUPATIONAL EXPOSURE; PREVENTION

<155>

Maltoni, C., Occupational carcinogenesis., In: Cancer Detection and Prevention, Proc. 2nd Int. Symp., April 9-12 (1973), Bologna, Intern. Congress Series No. 322. Excerpta Med., Amsterdam 2: 1-8 (1974).

Oncogenic factors are increasingly being produced and distributed in occupational environments, spreading to the general environment to become an ecological problem. Occupational carcinogenesis is a difficult field because the workers' health often conflicts with productive interests of the factories. The scientific community must recognize occupations which present an oncogenic risk, identify the causative agent, and assess the degree of risk. Methods of prevention include: 1) testing of all newly used agents, 2) up-to-date epidemiological data from workers exposed, 3) legislative measures forbidding production and utilization of agents shown to be oncogenic, 4) technical protection when weak or doubtful carcinogens are produced or employed, and 5) medical checks for early detection of preneoplastic lesions and tumors, as well as for the quantitative evaluation of risks. The value of medical checks may be over-emphasized, for the chief value may be to evaluate the epidemiological risk.

#### CARCINOGENICITY; EPIDEMIOLOGY; OCCUPATIONAL EXPOSURE

<156>

Maltoni, C.; Lefemine, G., The potential of the planned experiment in the prediction of the risk of ambient carcinogens. An example: Vinyl chloride., Atti Accad. Naz. Lincei, Cl. Sci., Fis., Mat., Nat., Rend. 56: (Series 8, fasc. 3) 1-11 (1974).

A wide variety of experiments were planned to verify the action of vinyl chloride (VC) in relation to the route of administration, dosage, duration, time and rhythm of treatment, type of test animal, age of the animal, and passage across the placenta. Especially constructed apparatus permitted exposures from 50 to 30,000 ppm and the simultaneous treatment of 1,200 experimental animals. The following points are indicated by the study: 1) VC is oncogenic and produced cancer of the zymbal glands, nephroblastomas and angiosarcoma in rats, and pulmonary adenoma-adenocarcinoma, mammary cancer, and hepatic angiosarcoma in mice. 2) There is a relation between dosage and response. 3) The nephroblastomas and zymbal gland tumors may be bilateral. 4) The liver angiosarcomas are polycentric. 5) Frequent vascular changes consisting of distypical and/or atypical endothelial proliferation occurred in treated animals. 6) Three ossifying angiosarcomas suggest new interpretations of acroosteolysis in the action of VC. 7) No acroosteolytic lesions had been observed at the time of the report. In conclusion, mandatory carcinogenicity testing must be done before approval of the admission of new reagents to the industrial or general environment.

Ital.; Eng. Transl.

#### CARCINOGENICITY; RAT; MICE; HAMSTER

<157>

Maltoni, C.; Lefemine, G., Carcinogenicity bioassays of vinyl chloride: Current results., Ann. N.Y. Acad. Sci. 246: 195-218 (1975).

Inhalation experiments with rats at exposures of 10,000, 6,000, 2,500, 500, 250, and 50 ppm vinyl chloride (VC) extended for 135 weeks. A new series of experiments (No. 15) with exposures of 25, 10, and 5 ppm has been started. Current results indicate that VC produced tumors in rats, mice, and hamsters, and that tumors of different types may be present in the same animal. The range of induced tumors varies to some extent from species to species, and several are quite rare or exceptional. A carcinogenic effect is exhibited at 50 ppm, and dose-response relationship is clear: from 500 to 50 ppm for angiosarcoma and from 250 to 50 ppm for nephroblastoma. Neoplastic response is also affected by the length of exposure and by the strain of rats used. Two subcutaneous angiosarcomas in offspring of breeder rats exposed for 7 days during pregnancy appear to indicate a transplacental effect of VC. No acroosteolytic lesions have appeared to date, but the observation of a few cases of ossifying angiosarcomas suggest a new orientation in the pathogenetic interpretation of acroosteolysis in workers exposed to VC. The results reported are considered to be both preliminary and incomplete as experiments are still in progress and more profound examinations are underway.

#### CARCINOGENICITY; RAT; MICE; HAMSTER

<158>

Maltoni, C.; Lefemine, G., Carcinogenicity bioassays of vinyl chloride. I. Research plan and early results., Environ. Res. 7(3): 387-405 (1974).

Vinyl chloride (VC), 99.99% pure, was administered to Sprague-Dawley rats, Wistar rats, Swiss mice, and hamsters, by inhalation, ingestion, endoperitoneal and subcutaneous injections, and transplacentally by exposure of breeder rats. Exposure concentrations varied from 50 to 30,000 ppm for 4 hrs per day, 5 days per week for varying numbers of weeks. Preliminary results indicate a direct relationship between dose and length of administration and the neoplastic response. Rats inhaling VC developed Zymbal gland carcinomas, nephroblastomas, and angiosarcomas of the liver and other anatomical sites; mice developed pulmonary adenomas, mammary carcinomas, and liver angiosarcomas. Blood vessel ectasias and endothelial hyperplasia were often observed. No acroosteolytic lesions developed, but the onset of 2 ossifying angiosarcomas suggests a new interpretation of acroosteolysis in VC workers. No tumors occurred in animals inhaling 50 ppm VC, in controls with no treatment, or in controls treated with 2500 ppm vinyl acetate. Both European and American manufacturing groups were apprised of the preliminary results of the experiment.

#### RAT; MICE; HAMSTER; CANCER; ANGIOSARCOMA; ACROOSTEOLYSIS; LUNG; LIVER; CARDIOVASCULAR

<159>

Maltoni, C.; Lefemine, G.; Gualano, L., Preliminary report on the carcinogenicity bio-assays of vinyl chloride., Informal Fact-Finding Hearing on Possible Hazards of Vinyl Chloride Manufacture and Use. (February 15, 1974).

Vinyl chloride (VC) of analyzed purity was administered in concentrations from 30,000 to 50 ppm simultaneously to 900 experimental rodents in specially constructed inoxidizable steel and glass test apparatus. Thirteen experiments were started in sequence: 1) 10,000, 6,000, 2,500, 500, 250, and 50 ppm of VC, 4 hrs/day, 5 days/wk, for 12 months. One group of untreated animals, and one group treated with 2,500 ppm vinyl acetate, were added as controls. 2) 200, 150, and 100 ppm VC. 3) As Exp. 1 but with shorter periods of exposure. 4) As Exp. 1 but with another species, mice, for 7 months. 5) Effects of exposure during pregnancy on offspring. 6) 30,000 ppm 4 hr/day, 5 days/wk, for 10 months--same as Prof. Viola's conditions. 7) As Exp. 1 but using another strain of rats, Wistar. 8) As Exp. 1 but with hamsters for 7 months. 9) Further

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assessment of VC at 50 ppm. 10) Effect of a high but short and/or intermittent exposure. 11) Effects of VC by ingestion. 12) To ascertain if VC acts on tissues directly or through metabolites. 13) Studies involving a third general route of exposure. Results: After 127 weeks, nephroblastomas, liver angiosarcomas, and cancers at various sites had been found in the groups exposed to 10,000, 6,000, 2,500, 500, and 250 ppm VC; Zymbal gland carcinomas had been found in rats receiving 10,000, 6,000, 2,500 and 500 ppm. The studies are continuing.

RAT; NICZ; MAMSTER; CANCER; ANGIOSARCOMA; LIVER

<160>

Mancuso, T.F., Cancer and vinyl chloride - polymerization implications, problems and needs., Internal Report, Industrial Union Department, AFL-CIO Unpublished

The need for a concerted effort relative to the problems posed by industrial chemicals -- the magnitude of the problem, the sources, and controls -- and the possibility of the development of an industrial epidemiological cancer surveillance system to aid in this effort are emphasized. The difficulties of diagnosis and medical evaluation, particularly in the small plants, may be magnified by inexperience and economic pressure. Insurance compensation laws need restudy. Recommendations for cooperation among industry, labor, government, and international organizations are proposed.

CANCER; OCCUPATIONAL EXPOSURE; INSURANCE  
COMPENSATION; EPIDEMIOLOGY

<161>

Mancuso, T.F., Comments for opening of discussion on "Neoplastic Effects", Ann. N.Y. Acad. Sci. 246: 251-257 (1975).

The significant medical observations reported on a single chemical complex and type of industrial exposure -- for example, vinyl chloride -- have focused on several areas of national and scientific interest: 1) whether the cancers observed will be confined to the manufacturing process, 2) nature and extent of the industrial medical surveillance, 3) epidemiological demonstration of an occupational cancer by histological type, 4) difficulties and limitations of records made on death certificates, 5) absence of necessary environmental data, and 6) the unknown potential of thousands of industrial chemicals and importantly the total absence of a national concerted study of occupational cancer. The observations on vinyl chloride provide striking evidence of the potential reservoir of carcinogenic agents in the work environment which have not been studied or investigated.

EPIDEMIOLOGY; OCCUPATIONAL EXPOSURE; DIAGNOSTIC;  
CARCINOGENICITY

<162>

Manufacturing Chemists' Association, Inc., Properties and essential information for safe handling and use of vinyl chloride., Chemical Safety Data Sheet, Manufacturing Chemists' Association, Inc. SD-56: 16p. (1954).

Vinyl chloride is a highly volatile, extremely flammable, compressed gas which is ordinarily handled in liquefied form under pressure. It has a mild anesthetic action with slow onset in concentrations above 500 ppm, and its vapors are irritating to the eyes and skin. Facilities for washing eyes for 15 minutes in running water and skin with copious quantities of water must be readily available. Prolonged contact with VC will result in refrigeration and freezing. Other precautions necessary in handling are: 1) keep away from heat, sparks, and open flame; 2) provide adequate ventilation; 3) ground equipment and

containers; 4) do not heat containers above 50 degrees C and no heat should be applied to tank cars; 5) all equipment should be made of steel and have a designed working pressure of at least 100-150 psi; 6) in the event of accidental leaks, spills, or excessive vapor concentrations only personnel equipped with approved respiratory protection should be permitted in the contaminated area; 7) chemical safety goggles should be worn when there is danger of the liquid or saturated vapor coming in contact with the eyes; and 8) waste disposal should be away from any source of ignition.

SAFETY; EXPLOSIVE; OCCUPATIONAL EXPOSURE; HUMAN;  
PROPERTIES

<163>

Marin, A.; Strauss, J.; Michiels, R.; Benoit, J.P.; Balthie, R.; Pierre, C., Acro-osteolyse d'origine professionnelle. [Acroosteolysis of occupational origin.], Rev. Rhum. 34(6): 340-351 (1967).

Five case studies of autoclave cleaners exhibiting acroosteolysis are presented with the results of clinical, radiological, and histological investigations. The lesion is concluded to be a vascular one complicated by bony resorption. A general chemical intoxication from occupational sources not yet completely identified is probable. An immunological dysfunction may be superimposed on a genetic susceptibility, and activated by a toxic chemical in certain individuals. No efficacious chemical therapy is known to date. Treatment is chiefly vaso-dilatory.

Fr.; Eng. Summ.

ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE; CASE STUDY

<164>

Markowitz, S.S.; McDonald, C.J.; Fethiere, V.; Kerzner, M.S., Occupational acroosteolysis., Arch. Dermatol. 106: 219-223 (1972).

Occupational acroosteolysis emerged as a new clinical entity in 1963. The disease is characterized by scleroderma-like lesions of the skin, conditions similar to Raynaud's phenomenon, and asymptomatic bony defects of the extremities; appears to be confined solely to workers engaged in the production of polyvinyl chloride from vinyl chloride; and is thought to occur in 3% or less of workers. Treatment is nonexistent with the only known preventive being removal from the environment. Two case reports of this unique disease are presented highlighting the incidence, cause, sequel, treatment, and prognosis.

CASE STUDY; CASE REPORT; REVIEW; HUMAN; SKIN;  
RAYNAUD'S PHENOMENON; BONE; OCCUPATIONAL EXPOSURE;  
ACROOSTEOLYSIS; POLYCLERER

<165>

Marsteller, H.J.; Leibach, V.K.; Mueller, R.; Gedick, P., Unusual splenomegalic liver disease as evidenced by peritoneoscopy and guided liver biopsy among polyvinyl chloride production workers., Ann. N.Y. Acad. Sci. 246: 95-134 (1975).

This excellent and extensive review of the literature between 1933 and 1973 covers prior studies of approximately 12,500 workers employed in vinyl chloride (VC) and polyvinyl chloride (PVC) polymerization and processing. Detailed case reports by the authors of 50 workers in VC and PVC plants include medical histories detailing anamnestic, clinical, biochemical, peritoneoscopic, and histologic data. Methods of investigation and illustrated findings are included. A bibliography of 163 references is appended.

REVIEW; CASE REPORT; BIBLIOGRAPHY; OCCUPATIONAL  
EXPOSURE; DIAGNOSTIC; LIVER

R&S 135424

<166>

Marsteller, H.J.; Lalbach, W.K.; Mueller, R.; Juehe, S.; Lange, C.-E.; Rohner, H.G.; Veltman, G., Chronisch-toxische Leberschaden bei Arbeitern in der PVC-Produktion. (Chronic-toxicity liver damage in workers in polyvinyl chloride production.), Deut. Med. Wochenschr. 98 (48): 2311-2314 (1973).

Forty-five male autoclave-cleaners from a polyvinyl chloride manufacturing plant were given extensive diagnostic laboratory, roentgenological, scintigraphic, and laparoscopic examinations because of 1) demonstrated alterations in the esophagus, 2) spleen enlargement, and 3) uncharacteristic alterations in the liver parenchyma as well as 4) difficult-to-classify sub-clinical liver damage. Of these, twenty men from 30 to 56 years of age with exposure durations to vinyl chloride ranging from 1 1/2 to 21 years were given further clinical and biochemical tests. Thrombocytopenia (16 cases), chronic liver damage (14 cases), splenomegaly (7 cases), and portal hypertension emerged as more significant symptoms of chronic toxicity than acroosteolysis (4 cases).

Ger.

POLYCLEANER; HUMAN; DIAGNOSTIC; BIOCHEMISTRY; LIVER; SPLEN; ACROOSTEOLYSIS

<167>

Mason, T.J., Cancer mortality in U.S. counties with plastics and related industries., Environ. Health Perspect. 11: 79-84 (1975).

Cancer mortality rates were calculated in individual counties of the U.S. utilizing the 1963 Census of Manufacturers for establishments primarily engaged in manufacturing plastics and other synthetic materials. Cancer mortality was low in the aggregate for many anatomic sites when compared to the total United States, but there were significant excesses in white males in some categories. For instance, in the plastics industries excesses appeared in lip, testes, eye, endocrine glands, and skin cancer other than melanoma. In the synthetic rubber industries the excesses were in nasal sinuses, lung, prostate, bladder, melanoma, and other skin cancer. Multiple myeloma was excessive in the synthetic fibers industries.

EPIDEMIOLOGY; CANCER; HUMAN

<168>

Mastrowatteo, E.; Fisher, A.H.; Christie, M.; Danziger, M., Acute inhalation toxicity of vinyl chloride to laboratory animals., Amer. Ind. Hyg. Assoc. J. 21: 394-398 (1960).

Exposure for 30 minutes to 10% vinyl chloride in air produced deep narcosis in mice and rats but no deaths. Thirty percent concentrations killed mice and rats. Exposure of guinea pigs to 20% produced deep narcosis, but 3 of 5 guinea pigs survived exposure to 40%. Pathological changes included congestion of the lungs with pulmonary edema and some hemorrhaging; failure of blood to clot; and congestion of liver and kidneys, with extensive fatty infiltration of the liver in 1 guinea pig. Survivors showed little pathological change.

RAT; MICE; GUINEA PIG; TOXICITY; BLOOD; LIVER; LUNG; KIDNEY

<169>

McCord, C.P., A new occupational disease is born., J. Occup. Med. 12(6): 234 (1970).

Acroosteolysis (AOL) was first reported in 1963, and appears to be confined to hand scrapers of reactor vessels in the polyvinyl chloride industry. Raynaud's phenomenon is characteristically the first manifestation, accompanied or followed by bony dissolution, generally confined to the distal ends of the fingers. Cause, portal of entry, and therapy

are not known.

ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE; RAYNAUD'S PHENOMENON; HUMAN; BONE;

<170>

McKinley, C.; Beckmann, R., Vinyl chloride. In: Control of hazardous material spills. Consideration of hazards associated with bulk sea transport of liquefied gases., Proceedings of the 1974 National Conference on Control of Hazardous Material Spills, August 25-28, 1974, San Francisco, California p 70 (1975).

Vinyl chloride presents a real danger in shipping; forms explosive acetylides with certain metals, and tends to polymerize with itself or to copolymerize with other monomers in the presence of air, sunlight, or heat, with an exothermic reaction which can be violent. Flammable mixtures of vinyl chloride vapor and air exist between 4 and 22% by volume, which produce carbon monoxide and hydrogen chloride on combustion. Recommendations include a) keep away from sparks, heat, and open flames; b) sufficient inhibitors should be present to prevent polymerization in storage and transport; c) avoid contact with aluminum, copper, bronze, brass, or other acetylide-forming metals; and d) prevent exposure to sun and oxygen.

SAFETY; NON-OCCUPATIONAL EXPOSURE

<171>

Myerson, L.B.; Meier, G.C., Cutaneous lesions in acroosteolysis., Arch. Dermatol. 106: 224-227 (1972).

A 36-year-old female--who had never worked in the vinyl chloride industry--exhibited idiopathic acroosteolysis with unique papular skin lesions. This seemingly nonoccupationally-related disorder is compared with selected literature on occupational acroosteolysis in vinyl chloride workers.

ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE; SKIN; CASE STUDY; HUMAN; RAYNAUD'S PHENOMENON; NON-OCCUPATIONAL EXPOSURE

<172>

Miller, A., Pulmonary function defects in nonsmoking vinyl chloride workers., Environ. Health Perspect. 11: 247-250 (1975).

Cigarette smoking must be considered in any investigation of air flow, and the smoking variable relative to the effect of atmospheric pollution and occupational exposure as causative factors in chronic nonspecific respiratory disease is of importance. A high prevalence of air flow impairment in vinyl chloride-polyvinyl chloride (VC-PVC) workers cannot be attributed to smoking. Prevalence in nonsmokers varied from 36.4% when occupational exposure to VC-PVC was less than 10 yr to 80% when exposure exceeded 20 yr. The latter is virtually the same as for smokers exposed more than 20 yr, and the same equivalency is apparent in workers over 40 years of age. For those less than 39 yr of age, however, 53% of smokers and 28% of nonsmokers exhibited reduced air flow. The difference in prevalence between smokers and nonsmokers narrowed from 23% when exposure was less than 10 yr to 11% when exposure exceeded 10 yr.

CIGARETTE SMOKING; EPIDEMIOLOGY; OCCUPATIONAL EXPOSURE; LUNG

<173>

Miller, A.; Teirstein, A.S.; Chuang, H.; Selikoff, I.J.; Warshaw, E., Changes in pulmonary function in workers exposed to vinyl chloride and polyvinyl chloride., Ann. N.Y. Acad. Sci. 246: 42-52 (1975).

Spirometry and maximal expiratory flow-volume curves from 148 workers in a vinyl chloride (VC) polymerization plant were examined in order to determine whether occupational exposure to VC gas

<173> CONT.

and polyvinyl chloride (PVC) dust is associated with changes in pulmonary function. A dilution in air flow was found in 200 workers or 57.5%. Prevalence of the diminution was similar in smokers and nonsmokers over 40 yrs of age or when exposure exceeded 20 yrs, thus suggesting an operative occupational factor. However, the findings do not determine whether VC or PVC is the more pathogenic. The fine dust of the polymer could concentrate in and damage small airways, or the dust and/or other small respirable particles could serve as carriers for VC monomer which could settle in the airways.

LUNG; OCCUPATIONAL EXPOSURE; EPIDEMIOLOGY; RESPIRATORY; HUMAN

<174>

Miller, F.D.; Jenks, D.P.; National Distillers and Chemical Corp., NY, Process for the manufacture of vinyl chloride., The Official Gazette of the U.S. Patent Office 744: 833 (1959).

A patent application for chlorination of ethylene to vinyl chloride, using the reaction of a solar excess of ethylene with chlorine in a temperature of 300 to 500 degrees C in the presence of ethylene dichloride in the proportion of 0.3 to 1 mole ethylene dichloride to 1 mole chlorine, was made on May 9, 1955 and granted on July 21, 1959. Patent number 2,896,000 was issued.

PATENT

<175>

Misgeld, V.; Stolpmann, R.-J.; Schulte, S., Zur Intoxikation durch Vinylchlorid-Polymerisate und/oder deren Begleitstoffe. (Poisoning by means of polyvinyl chloride or its constituents.), Z. Haut-Geschlechtskr. 48(11): 425-436 (1973).

The case study of a worker who had laid polyvinyl chloride (PVC) pipe for 10 yrs, and called it with PVC resin, is compared with similar case studies of acroosteolysis in the literature. The characteristic syndrome of scleroderma-like dermatosis, Raynaud's phenomenon, and bone defects led to a diagnosis of chronic toxicity by skin contact with either incompletely polymerized PVC, or with some additive in its composition.

Ger.; Eng. Summ.

TOXICITY; RAYNAUD'S PHENOMENON; ACROOSTEOLYSIS; SKIN

<176>

Monson, R.R., Proportional mortality among vinyl-chloride workers., Lancet 2(7894): 848 (1974).

It is desirable to compare disease ratios in a study group with those from a similar community in proportional-mortality studies, but tabulation of deaths in the United States are not available in specific enough detail to permit county-specific or state-specific comparisons. Average annual age-adjusted cancer mortality rates for Jefferson County, Kentucky compared with rates for the United States (as recently published by the U.S. Dept. of Health, Education, and Welfare) give no indication that use of proportional mortality for U.S. white males could account for the observed/expected ratio reported. (Monson, R.R., Lancet, 2(7877): 397-398 (Aug. 17, 1974)).

LETTER; MORTALITY

<177>

Monson, R.R.; Peters, J.M.; Johnson, M.M., Proportional mortality among vinyl-chloride workers., Lancet 2(7877): 397-398 (1974).

A proportional-mortality analysis of 161 deceased workers in 2 vinyl chloride plants revealed a 50% excess of deaths due to all cancer. Greatest excess was seen in liver, biliary tract, lung and brain.

Since 1970 over twice as many cancer deaths as expected have occurred.

CANCER; OCCUPATIONAL EXPOSURE; EPIDEMIOLOGY

<178>

Monson, R.R.; Peters, J.M.; Johnson, M.M., Proportional mortality among vinyl chloride workers., Environ. Health Perspect. 11: 75-77 (1975).

A 50% excess of deaths due to cancer was found in a proportional mortality analysis of 161 deceased workers in two plants using vinyl chloride. Heading the list of specific cancer sites are liver and biliary tract, lung, and brain. The excess in fatal cancer was seen mainly in men less than 60 years of age. More than twice the expected number of cancer deaths have occurred since 1970.

HUMAN; OCCUPATIONAL EXPOSURE; CANCER; LIVER; LUNG; BRAIN

<179>

Moslen, M.T.; Jaeger, R.J.; Szabo, S.; Reynolds, E.S., Acute inhalation toxicity of vinyl chloride monomer: Morphologic and biochemical effects of pretreatment with inducers of hepatic mixed function oxidase system., Abstracts of Papers for 14th Annual Meeting of Society of Toxicology, Williamsburg, Virginia, March 9-13 (1975) Abstract No. 28: p. 23-24 (1975).

As shown previously, acute hepatotoxicity of vinyl chloride monomer (VCM) is markedly enhanced by phenobarbital (PB) pretreatment and injury involves mainly the endoplasmic reticulum of liver parenchymal cells. Because one of the major effects of PB pretreatment is induction of certain components of the mixed function oxidase system (MPOS), correlation was attempted between induction of specific MPOS components and enhancement of hepatic injury by VCM. Rats were pretreated for 7 days with PB, Aroclor 1254 (1254), hexachlorobenzene (HCB), 3-methylcholanthrene (3-MC), spirocholactone (SNL) or pregnenolone-16-carbonitrile (PCN). Controls were given H<sub>2</sub>O by mouth. On the 8th day after a 16 hr fast animals were either sacrificed for determination of microsomal cytochromes b(5), P-448, P-450, NADPH-P-450 reductase and NADH-cytochrome-C reductase, oxidative-N-demethylase, and glucose-6-phosphatase, or exposed to 5% VCM for 6 hr and sacrificed 24 hr later. Liver injury was not apparent in H<sub>2</sub>O, SNL, 3-MC or PCN pretreated rats, while slight, moderate, and severe injuries were consistently found in HCB, PB and 1254 pretreated animals respectively. In animals pretreated with 150 micro-moles 1254/kg, a dose which nearly tripled P-450, VCM produced the most severe injury of the combinations tested. Although liver injury was only found in animals pretreated with an agent which induced P-450, induction of P-450 alone did not correlate with injury. PCN which induced P-450 did not potentiate VCM injury. Other cellular components in addition to P-450 may be important in the potentiation of VCM toxicity.

BIOCHEMISTRY; TOXICITY; RAT; LIVER; INTERACTION; PHENOBARBITAL; AROCLOR 1254; HEXACHLOROBENZENE; METHYLCHOLANTHRENE

<180>

National Fire Protection Association, Vinyl chloride - CH<sub>2</sub>CHCl, Fire Protection Guide on Hazardous Materials. 5th ed.: Section 49, 277 (1973).

Vinyl chloride (VC) is a colorless, sweet-smelling gas at ordinary temperatures, and is liquid below 7 degrees F. VC acts as a general anesthetic, may be fatal in high concentrations, is a skin irritant, and prolonged contact results in freezing due to rapid evaporation. It is flammable at ordinary temperatures, with flammable limits of 3.6% and 33%. Ignition temperature is 882 degrees F. The gas is heavier than air and may travel a considerable distance to a source of ignition and flash back.

<180> CONT.

Fires produce highly toxic combustion products such as hydrogen chloride and carbon monoxide. At elevated temperatures, as in fire conditions, polymerization may occur with possible container rupture. Self-contained breathing apparatus should be worn for personal protection. Storage should be outside or detached, in a cool, well-ventilated, noncombustible location, separate from oxidizing materials, and away from all possible sources of ignition.

SAFETY: PROPERTIES

<181>

National Institute of Environmental Health Sciences, Public health implications of components of plastics manufacture., Conference at Research Triangle Park, Pinehurst, NC July 29-31 (1974).

This timely conference was divided into 5 sessions: 1) Polymeric Materials: Manufacturing, Processing, and Additives. 2) Epidemiology and Toxicology: Vinyl Chloride. 3) Epidemiology and Toxicology of Polymeric Materials. 4) Toxicological and Environmental Aspects of Polymeric Materials. 5) Regulatory Aspects and Research Needs - Panel and Open Discussion. Representatives from university, industrial, and government organizations, as well as medical and public health authorities participated. Reports of the Conference are published in this issue of "Environ. Health Perspect."

CONFERENCE

<182>

New York Academy of Sciences, Working group: Toxicity of vinyl chloride-polyvinyl chloride., Conference, N.Y. Acad. Sci., New York, NY May 10-11 (1974).

This group of international participants working on various aspects of vinyl chloride (VC) held sessions on 1) Non-malignant Disease, 2) Experimental Observations (of non-malignant effects), 3) Neoplastic Effects, 4) Experimental Observations (Neoplasms), 5) Control of Exposure, and 6) Problems and Perspectives. Reports from this conference were published in the Annals of the New York Academy of Science, Volume 246.

CONFERENCE

<183>

Newsman, D.R., Ed., Tox. Mat. News Vol. 1: (1974).

This twice-monthly business newsletter published in Washington, D.C. was established to serve the interests of those concerned with the impact of chemical substances in the environment. Cited below are pertinent vinyl chloride events: 1(2): 15 (Apr. 1, 1974) B.P. Goodrich issues grant for vinyl chloride research. 1(3): 17 (Apr. 15, 1974) EPA may control vinyl chloride emissions from industrial plants. 1(3): 21 (Apr. 15, 1974) OSHA critical of EPA intent to permit vinyl chloride exposure in emergency rule. 1(3): 24 (Apr. 15, 1974) Grants, contracts and proposals. (Industrial/environmental hygiene surveys of vinyl chloride.) 1(4): 30 (May 1, 1974) Industry-sponsored tests indicate angiosarcoma in mice exposed to 50 ppm of VC. 1(4): 31 (May 1, 1974) FDA recalls sprays containing vinyl chloride. 1(5): 37 (May 15, 1974) Interview with Dr. Irving J. Selikoff, Part 1. 1(5): 35 (May 15, 1974) OSHA proposes "No Detectable Level" vinyl chloride standard. 1(5): 34 (May 15, 1974) Vinyl chloride meeting hears gloomy outlook for worker exposure to chemicals. 1(5): 33 (May 15, 1974) Manufacturing Chemists Association Board of Directors this week was giving final approval to a new study of vinyl chloride effects. (0 to 25 ppm). 1(7): 54 (June 15, 1974) B.P. Goodrich in midst of massive vinyl chloride research program. 1(7): 50 (June 15, 1974) EPA to continue exploring vinyl chloride emission standards. 1(13): 97 (Sept. 15, 1974) The Environmental Protection Agency Monday is expected

to release its task force report on vinyl chlorides. 1(13): 104 (Sept. 15, 1974) Bendix Launch Support Div., Cocoa Beach, Fla., receives contract for \$64,729 for environmental/industrial hygiene on vinyl chloride. 1(14): 106 (Oct. 1, 1974) OSHA sets final standards for worker exposure to vinyl chlorides. 1(14): 108 (Oct. 1, 1974) EPA Task Force Report on vinyl chloride: A special report. 1(15): 117 (Oct. 15, 1974) OSHA Vinyl Chloride Standard creates predictable result from industry, labor. 1(16): 122 (Nov. 1, 1974) EPA Vinyl Chloride Standards due in year, but monitoring problems remain.

<184>

Nicholson, V.J.; Hammond, E.C.; Seidean, H.; Selikoff, I.J., Mortality experience of a cohort of vinyl chloride-polyvinyl chloride workers., Ann. N.Y. Acad. Sci. 246: 225-230 (1975).

A cohort of 257 individuals, each of whom had been occupationally exposed to vinyl chloride (VC) for at least 5 yrs in a vinyl chloride polymerization facility, were studied by means of union and company records. Areas of investigation included: Major work activity during first 10 yrs of VC exposure, that is, reactor cleaning, maintenance, shipping; age at 10 yrs from first employment; Status of individuals exposed to VC for 5 or more yrs, that is, deceased, retired, working in production, working elsewhere; Expected and observed deaths from various causes; Causes of death; and Work Histories of individuals who had died of certain selected causes such as hemangiosarcoma. At least 17% of the deaths that occurred were causally related to exposure to vinyl chloride. Longer periods of observation are needed before concrete conclusions are made.

EPIDEMIOLOGY; OCCUPATIONAL EXPOSURE; HUMAN

<185>

Mitti, G.; Petruzzellis, V.; Pasano, V., Rheographic observations on workers in the plastics industry., Securitas 55: 683-694 (1970).

Twenty autoclave cleaners -- average age of 33 yrs (from 23 to 41 yrs) and an average work experience of 21 months (from 3 mos to 3 yrs) -- were given chest x-rays, hand x-rays, and laboratory examinations in addition to hemodynamic tests on the upper limbs by the duo-rheographic method, using a Schuffried apparatus coupled to a Schwarzler electrocardiograph. At 30 min intervals, rheographic traces were obtained under resting conditions, after cooling (by submerging the finger in crushed ice for five minutes), and after heating (submerging the finger in 40 degree C water for five minutes). A small degree of clinical symptomatology was found by contrast with the high percentage of rheographic alterations observed. In 14 out of 20 cases existence of sympathetic neurocirculatory dystonia attributable to a mechanical and/or chemical factor was found.

Ital.; Eng. Transl.

POLYCLEANER; DIAGNOSTIC; ACROOSTEOLYSIS; CARDIOVASCULAR

<186>

O'Mara, M.M.; Crider, L.B.; Daniel, R.L., Combustion products from vinyl chloride monomer., Amer. Ind. Hyg. Assoc. J. 32(3): 153-156 (1971).

Flame temperature of burning vinyl chloride monomer (VCM) varies with the amount of air premixing and ranges from 950 degrees C under diffusion conditions to 1466 degrees C with premixed air (120 to 190 cc/min) and VCM (65 to 90 cc/min). Soot or unburned carbon content varies from 3 to 6% of the VCM consumed, or 7 to 15% of the available carbon in the VCM molecule. An analysis of combustion gases reveals 27,000 ppm HCl; 58,100 ppm CO<sub>2</sub>; 9500 ppm CO; 40 ppm phosgene; and a trace of VCM. The quantity of hydrogen chloride is the main source of danger.

<186> CONT.

Dangerous amounts of phosgene may be present, but HCl will already have rendered the atmosphere insupportable. HCl odor serves as a warning device.

#### SAFETY; PROPERTIES

<187>

Occupational Safety and Health Administration, Informal fact-finding hearing on possible hazards of vinyl chloride manufacture and use., U.S. Department of Labor, Washington, D.C., 20210 Feb. 15, (1974).

Participants in this hearing on the possible hazards of vinyl chloride included personnel from the Occupational Safety and Health Administration and the National Institute for Occupational Safety and Health; industry representatives from B.F. Goodrich, Manufacturing Chemists Association, Dow Chemical Co., Franklin Electric Co.; labor representatives from the Oil, Chemical and Atomic Workers International, AFL-CIO, and United Rubber, Cork, Linoleum and Plastic Workers; medical specialists from the Mount Sinai School of Medicine, the Environmental Sciences Laboratory, the Instituto di Oncologia, Bologna, Italy, and the University of Pittsburgh Graduate School of Public Health; and an official of the Organization Resources Counsellors.

#### STANDARDS

<188>

Oster, G., Discussion of paper (Mefner, R.E., Jr., et al, *ibid.* pp 135-148), *Ann. N.Y. Acad. Sci.* 246: 149 (1975).

Serum albumin can transport vinyl chloride (VC) as demonstrated by the finding that VC displaces the fluorescent hydrophobic probe 1-anilinonaphthalene-8-sulfate bound to serum albumin and the system thus loses its fluorescence. Serum albumin is synthesized in the liver around the portal vein and may become localized, and may be metabolized via the cytochrome P-450 system in the endoplasmic reticulum of the liver cells. Liver microsomes will initiate polymerization of VC if the monomer concentration is high. Both monomer and free radicals are entrapped during the polymerization processes and may be released during warming, storage, exposure to sunlight, or during processing.

#### BIOCHEMISTRY; OCCUPATIONAL EXPOSURE

<189>

Oster, R.H.; Carr, C.J.; Krantz, J.C.; Sauerswald, M.J., *Anesthesia XVII. Narcosis with vinyl chloride.*, *Anesthesiology* 8: 359-361 (1947).

Two dogs, anesthetized using 50 vol % vinyl chloride momentarily and then reduced to 7 vol %, showed continuous "crowing", salivation, and uncoordinated leg movements. Recovery was prompt, with violent excitation. Four dogs, anesthetized using 10 vol % vinyl chloride maintained normal blood pressure during anesthesia but had intermittent tachycardia, extraneous systoles, and vagal beats. Electrocardiographic studies on six dogs at surgical anesthesia showed marked tachycardia followed by bradycardia. Abnormalities in the QRS complex in all six dogs varied from sinus arrhythmia to auriculoventricular block, ventricular multifocal extra systoles, and inversion of the T-wave. For these reasons vinyl chloride appeared unsafe as an anesthetic in the dog, and its use is unwarranted in man.

#### DOG; HUMAN; ANESTHETIC; CARDIOVASCULAR; NEUROLOGICAL

<190>

Partsch, H., *Ulceroskutierende Neuropathien der unteren Extremitäten.* (Mutilating ulcerous neuropathies of the lower extremities.), *Hautarzt* 22: 283-289 (1971).

This extensive literature review of acropathies with skin alterations, bony lesions, sensitivity disturbances, and crippling emphasizes the identity of the illnesses with known acroosteolysis foras. Case studies of familial origin, sporadic foras with their possible etiology, and diabetic neuropathies are presented. Occupational illnesses of workers in the vinyl chloride processing industries underscore the ambiguities of the etiological picture.

Ger.

#### HUMAN; CASE STUDY; ACROOSTEOLYSIS; EPIDEMIOLOGY

<191>

Patty, F.A. (Ed.), *Vinyl chloride.*, Industrial Hygiene and Toxicology, Vol. II. Toxicology. Interscience Publishers, New York Ch. 31, 1303-1305 (1963).

Uses, physical and chemical properties, and physiological responses of humans and test animals to vinyl chloride are reviewed. The principal response to vinyl chloride is central nervous system depression. Some lung irritation, but little kidney or liver damage, was observed on chronic exposure. Some hyperemia of liver and kidneys from acute exposure was noted. Clinical injuries from its extensive use in industry had not been reported. Available information on metabolism of vinyl chloride indicates that it is excreted by the lungs unchanged. The threshold limit set by the American Conference of Governmental Industrial Hygienists in April 1959 is 500 ppm. The sweetish odor is not adequate warning for excessive exposure. Fire and explosion are hazards. The explosive limits range from 4% to 22% by volume in air. Autoignition temperature is 472.22 degrees C.

#### PROPERTIES; NEUROLOGICAL; LUNG; KIDNEY; LIVER; STANDARDS; OCCUPATIONAL EXPOSURE; EXPLOSIVE; SAFETY

<192>

Patty, F.A.; Tant, W.P.; Waite, C.P., Acute response of guinea pigs to vapors of some new commercial organic compounds. V. Vinyl chloride., *Public Health Rep.* 45(2): 1963-1971 (1930).

Narcosis, ranging from unsteadiness to complete, is the principal symptom of vinyl chloride exposure in guinea pigs. A 40% concentration produced narcosis in 1/4 minute with death in 10 to 20 minutes. No symptoms were observed with concentrations of 0.5%. Lung irritation as well as hyperemia of kidney and liver were noted. Dizziness and disorientation were experienced by 2 humans exposed to 2.5% vinyl chloride for 3 minutes. Explosion represents a more serious hazard.

#### TOXICITY; GUINEA PIG; HUMAN; LUNG; KIDNEY; LIVER; EXPLOSIVE

<193>

Peoples, A.S.; Leake, C.D., The anesthetic action of vinyl chloride., *J. Pharmacol. Exp. Ther.* 48: 284 (1933).

First prepared in 1833, vinyl chloride is a gas at ordinary temperature with a boiling point of -13.9 C. It is heavier than air, with an ethereal odor, and burns with some difficulty in concentrations of 4 to 20% in air. Minimal anesthetic range on mice exposed for 10 minutes is 3.5 to 5 millimols in air; minimal lethal range for 10 minutes exposure is 10 to 12 millimols in air. At 7 millimols in air it anesthetizes rabbits and dogs within 1 minute. Recovery is rapid with no untoward effects.

#### PROPERTIES; ANESTHETIC; MICE; RABBIT; DOG

<194>

Perkel, G.; Mazzocchi, A.; Beliczky, L., Surveillance of workers with history of exposure to vinyl chloride., *Ann. N.Y. Acad. Sci.* 246: 311-312 (1975).

R&S 135428

## &lt;194&gt; CONT.

Industrial corporations are urged to join with unions in support of a Toxic Substances Control Act which would mandate the testing of all chemicals before they can be used in industry. Surveillance of workers in the vinyl chloride industry should include provision for medical examinations after the employee's exposure has ceased. Intensive research efforts are urgently needed to develop early-warning signs of disease and therapeutic techniques for treatment. Registries for employees exposed to carcinogens should be established by employers and transferred to the National Institute of Occupational Safety and Health for follow-up surveillance when the employee leaves the industry.

## OCCUPATIONAL EXPOSURE; INDUSTRIAL HYGIENE; UNION

## &lt;195&gt;

Petty, R., How surgeon's probe led to vinyl hazard findings., *Amer. Med. News* 17(21): 1, 12, 13 (1974).

In December, 1973, Dr. John L. Creech of Louisville, Ky., after attending a Goodrich employee who died of angiosarcoma and cirrhosis of the liver, searched company records and ascertained 4 cases of angiosarcoma within 6 years among 270 workers--a morbidity rate 100,000 times the national average. Findings were presented to the National Institute for Occupational Safety and Health (NIOSH) which, together with the Center for Disease Control, immediately began an epidemiological study. The first case had been diagnosed in 1961, 20 yrs after PVC was first industrially produced. Twelve yrs was the average time of handling vinyl chloride by workers who died of angiosarcoma: the shortest time was 4 yrs. High morbidity rates were also found for variously diagnosed ailments of liver, spleen, pancreas, and gallbladder. Suspecting a causal relationship, the Federal maximum on airborne vinyl chloride in PVC plants was immediately lowered to 50 ppa from 500 ppa set in the early 1960s when liver damage was found in rats exposed to 500 ppa. A most important reason for lowering the exposure limit was the direct suspicion that vinyl chloride caused acroosteolysis. In February, 1974, the U.S. Consumer Products Safety Commission banned the use of vinyl chloride as a propellant for household aerosol products. In May, 1974, an international meeting of scientists in New York presented an ominous picture of vinyl chloride toxicology which included liver damage, acroosteolysis, a wide variety of carcinomas, and a reticulated fibrosis tentatively identified as a precursor of cancer. In addition, "vinyl chloride disease" was found in 6 workers who had never worked in the polymerization process, but had made floor tiles from polyvinyl chloride, which apparently had enough residual vinyl chloride to cause illness.

## ANGIOSARCOMA; CANCER; ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE; HUMAN; LIVER; BONE

## &lt;196&gt;

Physical and Chemical Analysis Branch; National Institute of Occupational Safety and Health, Vinyl chloride in air., U.S. Government Printing Office 657-063/2035 P6CAM No. 178: 1-9 (1974).

A known volume of air is drawn through a charcoal tube to trap any vinyl chloride present. The charcoal is then transferred to a vial containing carbon disulfide where the vinyl chloride is desorbed. An aliquot of the desorbed sample is injected into a gas chromatograph and the resulting peak compared with a standard. The method is operational in a range of 0.2 to 1500 nanograms per injection, but the precision and accuracy of the method have not been determined. High humidity and competing substances in the sample may interfere with the analysis, but may be eliminated by altering chromatographic conditions. The sampling device is small, portable, and involves no liquids. The tubes are analyzed by an instrumental method, and two or more components in the sample may be investigated simultaneously. Disadvantages of the method are related to the limited amount of sample which can be

taken, and to the migration of volatile compounds such as vinyl chloride through the charcoal. This migration can lead to confusion as to the possibility of sample loss, but can be minimized by shipping and storing the tubes at -20 C.

## ANALYSIS

## &lt;197&gt;

Pluzhnikova, Z.I.; Kuz'micheva, M.M., (Hygienic assessment of polyvinyl chloride flooring for preschool institutions.), *Gig. Sanit. (Hyg. Sanit.)* 33(7): 50-53 (1968).

No vinyl chloride was detected in air samples from desiccators containing polyvinyl chloride tiles at 20 to 25 degrees C, or in the indoor air of children's institutions during the season when heating is used. Dibutylphthalate was detected in concentrations of 0.05 to 0.4 µg/m<sup>3</sup>. In addition, the polyvinyl chloride floor covering absorbed heat from the children's feet, and caused a buildup of static electricity on the surface of the palms.

Russ.; Eng. Transl.

## NON-OCCUPATIONAL EXPOSURE; DEPOLYMERIZATION

## &lt;198&gt;

Popov, L.A.; Tablochk, V. D., (Characteristics of gases released by polyvinyl chloride film.), *Gig. Sanit. (Hyg. Sanit.)* 32(7-9): 114-117 (1967).

Gases released during ageing and thermochemical degradation of polyvinyl chloride film included aldehydes, dimethyl phthalate, carbon dioxide, fatty acids, carbon monoxide, hydrocarbons, vinyl chloride, and hydrogen chloride. Depolymerization accompanied the processes of degradation which released gases in excess of the maximum permissible concentration for working premises at 20, 40 and 100 degrees C. At 100 C, 152 µg/m<sup>3</sup> vinyl chloride monomer was released in 1 hour from a 1 m<sup>2</sup> sample of polyvinyl chloride film.

Russ.; Eng. Transl.

## INDUSTRIAL HYGIENE; DEGRADATION; DEPOLYMERIZATION; STANDARDS

## &lt;199&gt;

Popper, H.; Thomas, L.B., Alterations of liver and spleen among workers exposed to vinyl chloride., *Ann. N.Y. Acad. Sci.* 246: 172-194 (1975).

A precursor stage to angiosarcoma -- characterized by a conspicuous subcapsular fibrosis, a nonpathognomonic progressive portal fibrosis, and a borderline increase of intralobular connective tissue, all associated with focal stimulation of sinusoidal lining cells and hepatocytes -- has been found in a preliminary review of hepatic biopsy and autopsy specimens obtained from workers in the vinyl chloride (VC) industry. This precursor stage is often accompanied by splenomegaly with enlarged Malpighian follicles and in some instances by portal hypertension. Transition to angiosarcoma is preceded by focal dilatation of sinusoids with activation but dedifferentiation of lining cells. This lesion is presumably the result of stimulation of various hepatic as well as splenic cells by VC or its metabolites. Frequency of the precursor lesion in relation to angiosarcoma is not established, but its detection is an indication of need to remove the worker from further exposure. Possible arrest of the progress of the lesion is still unclear.

LIVER; SPLEEN; CARCINOGENICITY; PRECURSOR; HISTOLOGY; PATHOLOGY

## &lt;200&gt;

Prodan, L.; Suciu, I.; Pislaru, V.; Ilea, E.; Pascu, L., Experimental acute toxicity of vinyl chloride (monochloroethene), *Ann. N.Y. Acad. Sci.* 246: 154-158 (1975).

## &lt;200&gt; CONT.

The acute toxicity (LD50) of vinyl chloride (VC) to mice, rats, guinea pigs, and rabbits was determined by 2 hr exposures to various concentrations of VC introduced at the lower part of the chamber at the beginning of the experiment and held for the test period without ventilation. The gas has no tendency to diffuse and high concentrations accumulate easily. Other experiments determined the lethality of VC when there was ventilation in the gas chamber, and when the gas in the chamber was constantly stirred. Lethal concentrations were 3 times lower when the gas was not stirred. Death was preceded by excitement, contractions and convulsions, accelerated respiration turning to Cheyne-Stokes respiration, followed by respiratory failure and death. Autopsy revealed general congestion of all internal organs. Some animals showed pulmonary edema, marbled liver, and slight tumefaction of the kidneys.

TOXICITY; RAT; MICE; GUINEA PIG; RABBIT

## &lt;201&gt;

Prodan, L.; Suciu, I.; Pislaru, V.; Ilea, Z.; Pascu, L., Experimental chronic poisoning with vinyl chloride (monochloroethene), Ann. M.Y. Acad. Sci. 246: 159-163 (1975).

Guinea pigs were exposed daily to 10% vinyl chloride (VC) for 90 days. A second group was exposed in the same way but received 10 mg of vitamin C in a solution of 20% sepharose administered orally with a pipette, which reduced the gravity of the lesions caused by vinyl chloride. Growth was diminished in poisoned animals with the exception of a group which was poisoned for 1 month and kept for 2 months before sacrifice, and in a group which was poisoned for 2 months and kept for 1 month before sacrifice. These two groups had better growth than the controls. No hematological changes were observed. Spontaneous motility was lessened due to the narcotic effect of VC. Significant differences in ascorbinaemia occurred, but vitamin C in the suprarenal glands showed no significant variations. Liver weight showed no significant differences as compared with body weight, but weight of the kidneys was significantly higher in all poisoned animals. Intense histopathological and histochemical lesions were present in liver, kidneys, spleen, and lungs. These lesions were confirmed by special staining methods.

TOXICITY; LIVER; KIDNEY; LUNG; SPLEEN; GUINEA PIG; VITAMIN C

## &lt;202&gt;

Pushin, G.A., (Lesions in the liver and bile ducts in workers producing some kinds of plastics), Sov. Med. 28(2): 132-135 (1965). (BA 47: 27890)

Examination of 350 workers in the Sverdlovsk Plastic Factory between 1957 and 1960 revealed that 15% of workers in the manufacture of polyvinyl chloride (PVC) had liver and bile duct disorders. Rolling-mill operators were the most frequently involved class, probably due to their exposure to decomposition products of PVC. The disorder was diagnosed as chronic epithelial hepatitis. In 9 of 23 patients, the hepatitis was associated with hypoaacidic or anacidic gastritis, in 15 with functional disturbances of the central nervous system, in 7 with thyroid disorders, and in 1 with hypochromic anemia.

Russ.

LIVER; NEUROLOGICAL; OCCUPATIONAL EXPOSURE; EPIDEMIOLOGY

## &lt;203&gt;

Rannug, U.; Johansson, A.; Rasmel, C.; Wachtmeister, C.A., The mutagenicity of vinyl chloride after metabolic activation., Ambio 3(5): 194-197 (1974).

The mutagenic effect of vinyl chloride (VC) on

*Salmonella typhimurium* was analyzed by means of reverse mutations in the histidine locus; metabolic activation of the VC molecule was studied by the addition of rat liver microsomal systems to the bacterial cultures. The microsomal system included the supernatant from the centrifuged liver homogenate of Sprague-Dawley rats, mixed with an NADPH-generating system consisting of NADP, glucose-6-phosphate, phosphate buffer, MgCl<sub>2</sub>, and KCl. VC was added as 1) gas dissolved in water, 2) gas dissolved in the microsomal system, and 3) exposure of the bacteria in the microsomal system to 1% vol/vol VC-containing atmosphere for 75 minutes at room temperature. A significant increase was found in the mutation rate after exposure to the VC gas, but not to the dissolved VC. Experiments without liver microsomes, or without NADP, elicited no mutagenic effect. Therefore metabolic activation by the microsomes appears to be required for the mutagenic effect, with the most plausible primary metabolite being chloroethylene oxide. Mutagenicity tests of the metabolites are under way. It is reasonable to assume that the carcinogenic action is also dependent on the same metabolite, and that the carcinogenicity of VC could have been predicted by mutagenicity testing.

MUTAGENICITY; CARCINOGENICITY

## &lt;204&gt;

Reed, A.B., Specialty propellant blends: Their evaluation and application to aerosols., Proc. Chem. Spec. Mfg. Assoc. Mid-Year Mtng. 48: 56-63 (1962).

Spray pattern of an aerosol depends upon the pressure of the package, and volume ratio of propellant to concentrate. Paint aerosols - including alkyd, lacquer, and acrylic systems - were tested for flammability, paint stability, container corrosion, and pigmentation, using different propellant blends, including vinyl chloride. Vinyl chloride formulations required more agitation, due to increased solvency and more settling. Polymerization was not a factor. Corrosion occurred in containers with systems containing vinyl chloride. Filling equipment and plant facilities must be evaluated to insure safe handling.

SAFETY; OCCUPATIONAL EXPOSURE; AEROSOLS

## &lt;205&gt;

Regnault, V., Ueber die Zusammensetzung des Chlorkohlenswasserstoffs. (The synthesis of chlorinated hydrocarbons.), Justus Liebig's Annalen der Chemie 14: 22-28 (1835).

While attempting to verify the formula for ethylene dichloride, Regnault observed a crystalline precipitate which formed in a mixture of ethylene dichloride and an alcoholic solution of potassium hydrate. When the containing receptacle was held in the hand, the liquid boiled evolving a gas with a decidedly ether-like smell which burned with a yellow flame with green edges, and was similar to ethyl chloride. He identified the precipitate as potassium chloride and, after further research, established the formula for the gas to be C<sub>2</sub>H<sub>2</sub>Cl<sub>2</sub>. It could be liquified at -15 to -18 degrees C, was soluble in alcohol and ether, and less soluble in water. This gaseous substance was later recognized as vinyl chloride.

Ger.

SYNTHESIS; ANALYSIS

## &lt;206&gt;

Reynolds, E.S.; Jaeger, R.J.; Murphy, S.D., Acute liver injury by vinyl chloride: Involvement of endoplasmic reticulum in phenobarbital-pretreated rats., Environ. Health Perspect. 11: 227-233 (1975).

Phenobarbital pretreated rats were exposed to 5% vinyl chloride (VC) for 6 hrs. Dilatation of the cisternae of the rough endoplasmic reticulum occurred in the centrilobular liver parenchyma; in

<206> CONT.

the smooth endoplasmic reticulum cisternae coalesced into discreet aggregates resembling denatured membranes. These results support the hepatotoxic hypothesis: VC conversion to a toxic metabolite by the mixed function oxidase system of liver endoplasmic reticulum.

**PATHOLOGY: RAT; PHENOBARBITAL**

<207>

Roemp. H., Vinylchlorid (Vinyl chloride.), Chemie Lexikon, Frank'sche Verlagshandlung, Stuttgart, Germany Band IV: 6933 (1966).

Properties of the vinyl chloride (VC) gas are summarized in a brief paragraph. VC was first described by Regnault in 1838; its polymerization capabilities were recognized in 1878, but were not utilized until 1933-1935. VC has been utilized in aerosol bombs since 1955. German patent numbers are listed. Manufacturers in Germany are: Allied Chemical; BASF; Dow; Dynamit AG.; Ethyl Corp.; Huels; Schuchardt.

Ger.

**PROPERTIES; MANUFACTURE**

<208>

Rothschild, L. Jr., Vinyl chloride news notes, Pest. Chem. News Sept. 1973 to Nov. 1974.

Detailed coverage and in-depth analyses, every week, of key developments regarding the laws and regulations governing pesticides and toxic chemicals. For the period September 1973 through November 1974 the following news items were released: 1(40): 2 (Sept. 5, 1973) Vinyl chloride monomer survey to document the health experience of workers. 2(11): 6 (Feb. 13, 1974). Emergency OSHA Standard for vinyl chloride and PVC possible. 2(12): 19 (Feb. 20, 1974). Industry claims emergency OSHA Standard for vinyl chloride unnecessary. 2(13): 17-18 (Feb. 27, 1974). 1). Permanent OSHA Standard for vinyl chloride, PVC may be effective in April. 2). EPA requested to suspend pesticides containing vinyl chloride as a propellant. 3). Fast implementation of OSHA Permanent Standard may satisfy worker groups. 2(15): 7 (Mar. 13, 1974). EPA is expected to act on HPG's vinyl chloride petition in about a month. 2(17): 10 (Mar. 27, 1974). OSHA to issue permanent and temporary vinyl chloride standards. 2(17): 2 (Mar. 27, 1974). Vinyl chloride petition filed by the Health Research Group (HRG) is expected to get an EPA response soon. 2(18): 18 (Apr. 3, 1974). EPA Vinyl Chloride Task Force members will brief public interest groups. 2(19): 25 (Apr. 10, 1974). EPA plans to release names of pesticides containing vinyl chloride April 15. 2(20): 21 (Apr. 17, 1974). Voluntary recall of pesticides containing vinyl chloride requested by EPA. 2(21): 20 (Apr. 24, 1974). EPA suspends 28 pesticides containing vinyl chloride. 2(21): 21 (Apr. 24, 1974). Suit filed to try to force release of names of all vinyl chloride pesticides. 2(22): 8 (May 1, 1974). Suspension order, notice of intent to cancel vinyl chloride pesticides issued. 2(22): 20-21 (May 1, 1974). 1). Vinyl chloride monitoring protocols being developed by EPA's ORD. 2). Vinyl Chloride Task Force could recommend regulatory action. 3). EPA asked to immediately measure vinyl chloride in air near plants. 4). OSHA Permanent Standard on vinyl chloride still pending. 2(23): 2 (May 8, 1974). Vinyl chloride and polyvinyl chloride toxicity will be the subject of a working group meeting in New York City May 10-11. 2(24): 5 (May 15, 1974). Scientists hear of vinyl chloride dangers: OSHA proposes permanent standard. 2(25): 5 (May 22, 1974). Vinyl Chloride Task Force aims at July 1 for regulatory recommendations. 2(26): 3 (May 29, 1974). More vinyl chloride pesticides suspended and brand names released. 2). EPA checks aerosols for more vinyl chloride pesticides. 2(26): 21-22 (May 29, 1974). EPA may recommend above zero air levels of VC; OSHA schedules hearing. 2). EPA Task Force wants to review actions, draft

recommendations. 2(27): 3 (June 5, 1974). Vinyl chloride air emission data requested by EPA from 27 firms. 2(28): 13-16 (June 12, 1974). 1). Vinyl chloride plant emissions not imminent hazard, Train says. 2). MCA begins four new research programs on vinyl chloride. 3). Firm requests hearing on suspension/cancellation of vinyl chloride pesticide. 4). Vinyl chloride pesticide recall estimated at 271,900 units. 2(29): 7 (June 19, 1974). 1). FDA tells consumers PVC data show low monomer levels with current uses. 2). Final EPA vinyl chloride air emission standard could be issued in 10 months. 2(30): 10 (June 26, 1974). 1). Report estimates 239.92 pounds of VCM emissions per hour from one plant. 2). OSHA's vinyl chloride standard will destroy industry's "viability", SPI claims. 2(32): 5-6 (July 10, 1974). 1). EPA suspends 14 more vinyl chloride containing pesticides. 2). OSHA Vinyl Chloride Standard hearings continue this week. 3). OSHA's draft environmental impact statement on the Standard notes its "adverse consequences". 2(33): 12 (July 17, 1974). 1). EPA vinyl chloride regulation nears; monitoring reports filed by Regions 2, 3. 2). Tenneco plant in Region 2 has VCM air emissions of 8,6000 pounds/day, report says. 2(34): 11-14 (July 24, 1974). 1). Vinyl chloride research plans discussed by seven agencies. No known technology to remove VCM from air streams, firm says. 2(35): 12 (July 31, 1974). Conclusions in OSHA draft EIS on vinyl chloride standard not supported, says SPI. 2(36): 11 (Aug. 7, 1974). Landfilling PVC solid wastes is probably not an acceptable disposal method. 2(38): 6 (Aug. 21, 1974). OSHA draft EIS on proposed vinyl chloride standard is "superficial", EPA says. 2(39): 13 (Aug. 28, 1974). 1). Senate hearings on vinyl chloride emphasize need for toxic substances bill. 2). EPA outlines goals in control of vinyl chloride emissions. 2(42): 13-16 (Sept. 18, 1974). Train orders implementation of all Vinyl Chloride Task Force recommendations. 2(43): 2 (Oct. 9, 1974). Vinyl chloride final standards set out by OSHA in the Oct. 4 Federal Register. 2(46): 8-9 (Oct. 16, 1974). 1). PVC air monitoring to start near two plants in the southeast. 2). Vinyl chloride used again to press for Toxic Substances Control Act. 2(47): 25-26 (Oct. 23, 1974). Vinyl chloride finite ambient air standard not yet possible, EPA paper says. 2(49): 4-6 (Nov. 6, 1974). Industry must act to prevent vinyl chloride type incidents, Schweitzer says.

**PESTICIDE; TOXICITY**

<209>

Rothschild, L. Jr., Vinyl chloride news notes, Food Chem. News June 18, 1973 to Oct. 28, 1974.

A weekly Washington publication for executives providing in depth information regarding regulation of food additives, colors, pesticides, and allied products. News headings from June, 1973 to October, 1974 are listed as search parameter guides: 15(13): 7 (June 18, 1973). Continued use of polyvinyl chloride resins in alcohol-contacting gaskets asked. 15(17): 2 (July 16, 1973). Polyvinyl chloride proposal to eliminate the prior sanction for use in packaging alcoholic beverages. 15(35): 13 (Nov. 19, 1973). EPA comment on PVC proposal suggests limiting vinyl chloride monomer. 15(40): 22 (Dec. 24, 1973). Full and complete testing of PVC resins and bottles urged by firm. 15(50): 25-26 (Mar. 4, 1974). FDA Asks SPI for further data on polyvinyl chlorides 15(52): 23-24 (Mar. 18, 1974). FDA may revoke prior sanction for PVC food packaging. 16(2): 5 (Apr. 1, 1974). Interim food additive order for PVC would set limits. 16(3): 3 (Apr. 8, 1974). Schaidt says FDA is concerned about PVC food packaging. FDA has begun collecting data from industry, other governments. 16(3): 2 (Apr. 8, 1974). Vinyl chloride use in aerosol food products. 16(6): 20 (Apr. 29, 1974). PVC proposal will limit VCM by end test, but not in resin. 16(8): 2 (May 13, 1974). Vinyl chloride industrial exposure limit. 16(13): 3 (June 17, 1974). Vinyl chloride industrial exposure limit. Ronk says PVC data show low monomer levels with current uses. 16(22): 25-26 (Aug. 19, 1974). PVC Document being readied for publication. 16(29): 15-16 (Oct. 21, 1974). 1). FDA revises PVC proposal

<209> CONT.  
to set two food uses. 2). VCM static extraction tests from PVC pipe reported by firm. 16(31): 17-18 (Oct. 21, 1974). Schaffner describes PVC regulatory situation. 16(32): 43-44 (Oct. 28, 1974). 1). FDA policy on PVC food uses delayed for coordinated agency view. 7). Johns-Manville says VCM method can be used only in water.

<210>  
Pouques, L., L'acro-osteolyse dans l'industrie des matieres plastiques. (Acroosteolysis in the plastics industry.), Presse Med. 75(37): 1848 (1967).

A case study of a worker in a polyvinyl chloride polymerization plant revealed symptoms similar to Raynaud's phenomenon as well as cold sensitivity and clubbing in the fingers, and to a lesser extent in the toes. No skin changes were observed. Massive osteolysis of the terminal phalanges was seen on radiological examination. Other workers who handled the raw materials of the polymer were not affected.

Fr.

PATNAUD'S PHENOMENON; ACROOSTEOLYSIS; BONE; OCCUPATIONAL EXPOSURE

<211>  
Rove, V.K., Experience in industrial exposure control., Ann. N.Y. Acad. Sci. 246: 306-310 (1975).

Methods available for environmental monitoring of air for the presence of vinyl chloride are: 1) gas chromatography, 2) total hydrocarbon analyzer with flame ionization detector, 3) combustion-conductivity, and 4) infrared spectrophotometry. Dow utilizes combustion-conductivity analyzers coupled to computer output, continuous gas chromatography units, and portable instruments based on infrared spectrophotometry. Personnel monitoring is achieved through use of absorption tubes filled with activated carbon followed by gas chromatography of absorbed chlorinated hydrocarbons. Breath analysis is a less used method. Some of the plant design and engineering principles recommended are: 1) closed processing systems, 2) open-air buildings for VC manufacture or polymerization, 3) reasonable process automation and remote operation, 4) closed-loop sampling systems with on-line monitoring, 5) specially designed vapor equalizing lines for loading of tank cars, 6) continuous environmental monitoring, 7) cleaning of reactor vessels by water jets -- followed by blanking of all entry lines, with assured oxygen supply, continuous vinyl chloride monitoring probe, and air purge during entry and cleaning of the vessel.

MANUFACTURE; SAFETY; OCCUPATIONAL EXPOSURE

<212>  
Rumyantseva, E.P.; Goryacheva, L.A., (Glucocorticoid function of the adrenals in patients suffering from chronic poisoning with some unsaturated and chlorinated hydrocarbons.), Gig. Tr. Prof. Zabol. 12(12): 16-19 (1968).

Adrenal function was substandard in a group of 105 patients with chronic poisoning by unsaturated and chlorinated hydrocarbons (including vinyl chloride). After 20 ACTH units, the Thorn test proved negative in 33%; in 35.8% ACTH failed to produce leucocytosis; in 73% the reaction of 17-oxy corticoids was either negative or perverted.

Russ.; Eng. Summ.

HUMAN; OCCUPATIONAL EXPOSURE; BIOCHEMISTRY; CASE STUDY; ADRENAL

<213>  
Sakabe, H., Bone lesions among polyvinyl chloride production workers in Japan., Ann. N.Y. Acad. Sci. 246: 78-79 (1975).

The first case of occupational acroosteolysis in Japan was reported in 1972 in a polyvinyl chloride (PVC) reactor cleaner who had cleaned reactors from 1960 to 1964. Also in 1972 the Ministry of Labour requested health examinations of all PVC workers in polymerization processes. From 1599 workers, x-ray examinations revealed 2 clear-cut cases of occupational acroosteolysis, with 48 suspected cases. A standard of diagnosis has since been established and distributed in an effort to improve x-ray examinations. The threshold limit value for vinyl chloride (VC) has been reduced to 200 ppm. Exposure has been reduced by means of protective clothing, improved methods of reactor cleaning, and shortened working hours. A thorough epidemiological study among workers in VC and PVC plants in Japan is planned.

BONE; OCCUPATIONAL EXPOSURE; POLYCLEANER; STANDARDS; ACROOSTEOLYSIS; CASE REPORT

<214>  
Sax, N.I., Vinyl chloride., Dangerous Properties of Industrial Materials, Van Nostrand Reinhold Co., New York 3rd ed., pp. 1227-1228 (1969).

Vinyl chloride--chloroethylene or chloroethene--with a formula of CH<sub>2</sub>CHCl is a colorless gas, or liquid when inhibited, with a faintly sweet odor. It has the following constants: Molecular weight: 62.50; boiling point: -13.4 C; lower explosive level: 4%; upper explosive level: 22%; freezing point: -159.7 C; density of liquid: 0.9155 at 15 C, referred to water at 4 C; vapor pressure: 2600 mm at 25 C; vapor density: 2.15; autoignition temp: 882 F. It is moderately irritating both to the lungs and by local application, causing skin burns or frostbite. Its chronic effect on the system is unknown in humans, but it causes liver injury in rats and rabbits. Circulatory and bone changes are reported in workers handling the monomer. Threshold limit value is 500 ppm or 1290 mg/m<sup>3</sup>. It is a fire hazard when exposed to heat or flame, and is difficult to extinguish. Explosion hazard is high. When heated it emits toxic fumes of phosgene.

EXPLOSIVE; SAFETY; OCCUPATIONAL EXPOSURE; PROPERTIES; SKIN; LIVER; HUMAN; BONE

<215>  
Schaffner, R.M., FDA and the vinyl chloride problem - An overview., Association of Official Analytical Chemists Meeting, Washington, D.C. 11 pages (October 15, 1974).

Polyvinyl chloride (PVC) was approved by the Food and Drug Administration (FDA) as a food packaging material on the basis, from available analytical data, that the resin was insoluble in food-simulating solvents, and that it did not migrate into the food. In 1971, levels of 10 to 20 ppm vinyl chloride (VC) were found in liquor packaged in PVC bottles, and data indicated that VC could also migrate into non-alcoholic foods. In 1974, deaths from angiosarcoma, supposedly due to VC were announced, and research on rats showed tumors developed at 250 ppm level of inhalation. In April 1974, FDA requested recall of products using VC as a propellant, and their ban was published in the U.S. Federal Register. EPA banned VC as a propellant in pesticide aerosol propellants and instituted environmental surveys. Reports of angiosarcoma and other tumors in rats inhaling 50 ppm VC were released by Prof. C. Maltoni. In June 1974, angiosarcoma was diagnosed in employees of the PVC fabricating industry. Residual levels of VC in PVC vary depending on the processing, particle size and porosity, and drying methods. Basic resin may contain levels from several to 2000 ppm, and the final product may contain anywhere from less than 1 to several hundred ppm. Work directed toward the appraisal of carcinogenicity of VC by the oral route is in progress. A low residual monomer content is indicated in thin films and highly plasticized articles. Preliminary results in methodology development indicate that VC may be determined at

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levels of 50 ppb in vegetable oils and food-simulating solvents representing aqueous, acidic, alcoholic, and fatty foods, and at 1 ppm in the PVC plastic itself.

ANALYSIS; NON-OCCUPATIONAL EXPOSURE; FOOD; AEROSOLS

<216>

Schanche, D.A., Vinyl chloride: Time bomb on the production line., *Today's Health* 52(9): 16-19, 70-72 (1974).

Health hazards of vinyl chloride were first brought to the attention of the American public when J.L. Creech discovered a cluster of rare angiosarcoma cases among the workers of B.F. Goodrich's Louisville, Kentucky plant. Urgent medical inquiries began. Subsequently various investigating groups mobilized: the Occupational Safety and Health Administration (OSHA) of the Department of Labor; the National Institute for Occupational Safety and Health (NIOSH); the Environmental Protection Agency (EPA); the Center for Disease Control (CDC); the National Institutes of Health (NIH); the American Cancer Society (ACS); the Environmental Science Laboratory, Mount Sinai School of Medicine, New York. An emergency standard of 50 ppb has been set. The vinyl chloride industry stated that a proposed permanent standard of no detectable level is not feasible and if adopted will shut down the entire plastics industry. On the other hand, a worker representative threatens a shutdown if the proposed permanent standard is not adopted. One company has reportedly reduced levels to as low as 1 to 5 ppb. Three fatal cases of non-occupational exposure to vinyl chloride have occurred in New York State. The EPA estimates 300 million pounds of vinyl chloride escapes into the atmosphere each year.

STANDARDS; OCCUPATIONAL EXPOSURE; NON-OCCUPATIONAL EXPOSURE; CANCER; LIVER; ANGIOSARCOMA

<217>

Schaumann, O., Effect on the heart of some inhalation anaesthetics., *Medizin. Chemie* 2: 132-140 (1934).

Ether, chloroform, solasethin (CH<sub>2</sub>CHCl), and vinyl chloride (VC) were tested to determine the concentrations injurious to the heart of the cat. Relative insufficiency of the heart was measured by the auricular pressure; and the limiting concentration at which absolute insufficiency occurred was also measured. In comparison with ether (3 vol %), vinyl chloride required 19 vol % for the same relative insufficiency. Ether caused complete insufficiency at 12 vol %, but absolute insufficiency was not possible with VC, even with 25 to 30 vol %. The concentration of VC in the blood during anaesthesia is 15 to 17 mg % as compared with chloroform at 30 to 50 mg %, although a concentration of chloroform 10 times higher than VC is required for anaesthesia. The ratio of anesthetic to toxic concentration is the most favorable for vinyl chloride of those anesthetics tested.

ANESTHETIC; CAT; CARDIOVASCULAR

<218>

Schmidt, A.M., Human drugs containing vinyl chloride or packaged in polyvinyl chloride containers., *Fed. Register* 39(78): 14238 (April 22, 1974).

Each registrant under section 510 of the Federal Food, Drug, and Cosmetic Act is required to submit to the Food and Drug Administration a list of all human drugs which are being manufactured, prepared, propagated, compounded, or processed for commercial distribution and which contain vinyl chloride whether or not the vinyl chloride is an active or inactive ingredient, and a list of all human drug products packaged in polyvinyl chloride containers or in containers with polyvinyl chloride liners. Information was to be submitted by May 22, 1974.

REGULATION; HUMAN; DRUG

<219>

Schneidersman, M.A.; Mantel, N.; Brown, C.C., From mouse to man -- or how to get from the laboratory to Park Avenue and 59th Street., *Ann. N.Y. Acad. Sci.* 246: 237-248 (1975).

The extrapolation of moderate or high dose animal toxicity data to presumed effects in man may be very dangerous, and must be done cautiously. Even the extrapolation from small or medium-sized experiments at high-dose levels to the very low dose levels where large numbers of animals are required is full of risks. Extrapolation within species using four common mathematical modelling methods and the Manton liver angiosarcoma data as examples are discussed, and the difficulties of using models for low-dose effects are elucidated. The models involving time-to-response need more development as most of them are concerned with median time to appearance of cancer while the present need is the time for 1 or 0.1% to develop cancer. Problems include inherent observational problems, mathematical problems, competing risks, interaction of materials, natural incidence, methods for including nonexperimental evidence as data, and the establishing of acceptable risk levels. Extrapolation from one species to another involves differences in dose-size relation, metabolic rate, the ratio of blood volume to circulation time, tissue binding, generation time of cells, rate of repair processes, and degree of environmental control. Appropriate research on species differences in metabolism and in the mathematics of modeling and extrapolation are needed. Also important is free and open discussion of the socially related issues -- acceptable risk as well as the costs and benefits to both the individual and to society.

EPIDEMIOLOGY; MODEL; STATISTICS

<220>

Schottek, W., Zur Toxikologie des Vinylchlorids. (Toxicology of vinyl chloride.), *Chem. Tech.* 21(11): 708-711 (1969).

Mice, rats, and guinea pigs survived a 200,000 ppm vinyl chloride exposure, but showed edema of the lungs and congestion of the liver. At 70,000 ppm guinea pigs lapsed into deep narcosis with severe irritation of the eyes and respiratory organs. In rats, 100 ppm exposure for 7 hours per day over 6 months produced liver enlargement. In humans, concentrations of 1,000 to 25,000 ppm produced central-nervous-system disturbances ranging from slight dizziness through sleepiness and nausea to severe vertigo, disorientation, headache and visual disturbance. A brief review of the literature is presented.

Ger.

TOXICITY; RAT; MICE; GUINEA PIG; HUMAN; OCCUPATIONAL EXPOSURE; STANDARDS

<221>

Schweitzer, G.E., Environmental concerns beyond the workplace., *Ann. N.Y. Acad. Sci.* 246: 296-302 (1975).

The Environmental Protection Agency (EPA) suspended the use of pesticides in enclosed areas with a mandatory recall of stocks in the market, and is investigating the need and authority for further regulatory action. An excess of 200 million pounds of vinyl chloride (VC) and 50 million pounds of polyvinyl chloride (PVC) is released annually to the environment. Epidemiological studies of populations near the chemical plants producing VC and PVC are needed. Also needed are toxicological tests detailing the likely health effects of VC in ambient air near these chemical plants, and research to clarify the toxicological significance of impurities in VC, synergistic effects of other chemicals, and metabolic reactions induced by VC. In addition to

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the immediate concern with ambient and peak levels of VC near chemical plants, EPA is concerned 1) with the VC level in water and sludge, 2) with developing sampling and analysis procedures, 3) with the persistence of VC, 4) with the migration of VC from PVC, and 5) with the disposal of PVC. Passage of the Toxic Substances Control Act would greatly assist the EPA in these concerns.

ENVIRONMENT: NON-OCCUPATIONAL EXPOSURE; ANALYSIS

<222>

Schwetz, B.A.; Leong, B.-K.J.; Smith, P.A.; Balser, M.; Gehring, P.J., Results of a vinyl chloride-teratology study in mice, rats, and rabbits., Abstracts of Papers for 14th Annual Meeting of Society of Toxicology, Williamsburg, Virginia, March 9-13 (1975) Abstract No. 29: p. 25 (1975).

The deleterious potential of inhaled vinyl chloride monomer (VCM) was evaluated on the developing embryo and fetus of mice, rats, and rabbits exposed to 500 ppm VCM 7 hr daily during organogenesis. Some of the VCM-exposed mice were also treated with 15% ethanol (EtOH) in the drinking water to determine if ethanol ingestion altered the toxicity and/or teratogenicity of VCM. No signs of toxicity were observed in the adult rats or rabbits during exposure or at the time of necropsy and cesarean section. A significant decrease was seen in rat fetal body weight; in both rats and rabbits the incidence of external, soft tissue and skeletal malformations was not different from control litters. Mice were more susceptible to VCM than either rats or rabbits. A slight decrease in weight gain was recorded among mice and maternal deaths were observed (6 deaths/30 exposed mice). Pregnancy rate among mice was slightly lower than among controls; a slight increase was observed for resorptions and fetal body weights were somewhat lower than control values; but the incidence of external, soft tissue, and skeletal malformations was not different from controls. Concomitant treatment of mice with EtOH in the drinking water accentuated some of the toxic effects associated with exposure to VCM alone. Maternal weight gain and pregnancy rate were further decreased, but the incidence of maternal deaths was not increased by concomitant EtOH ingestion. The incidence of cleft palate and certain skeletal anomalies was significantly increased among mice receiving EtOH plus VCM. Thus, based on the results of this initial study, exposure of bred mice, rats, and rabbits to 500 ppm VCM during organogenesis did not result in a teratogenic response.

TERATOGENICITY; RAT; MICE; RABBIT; INTERACTION; ETHANOL

<223>

Selikoff, I.J. (Ed.); Hammond, E.C. (Ed.), Toxicity of vinyl chloride-polyvinyl chloride., Ann. N.Y. Acad. Sci. 246: 1-337 (1975).

This volume results from a workshop held at the New York Academy of Sciences on May 10 and 11, 1974. The contents include Part I. Toxicological Investigations of Vinyl Chloride-Polyvinyl Chloride: A. Clinical Studies (10 papers), B. Experimental Studies (7 papers), and C. Pathology (1 paper); Part II. Carcinogenesis Associated with Vinyl Chloride: A. Experimental Studies (2 papers), B. Epidemiological Studies (6 papers), and C. Pathology (2 papers); Part III. Environmental Considerations (2 papers); Part IV. Control and management (2 papers); and a bibliography.

CONFERENCE

<224>

Svirnova, N.I.; Granik, V.P., (Long-term side effects of acute occupational poisoning by certain hydrocarbons and their derivatives.), Gig. Tr. Prof. Zabol. 14(5): 50-51 (1970). (RA52: 46328)

Two case studies of vinyl chloride poisoning are included in this report. The frequency and degree of expression of 1) functional disturbances of the central nervous system (CMS) 2) sympathetic-sensory polyneuritis, and 3) organic disorders of the brain, which were seen as residual effects of the poisoning, depended upon the severity of the intoxication, previous CMS diseases, and the time of recovery before returning to work.

Russ.

OCCUPATIONAL EXPOSURE; HUMAN; NEUROLOGICAL

<225>

Smith, D.L.; Giesler, V.S., An evaluation of organic vapor respirator cartridges and canisters against vinyl chloride., National Institute for Occupational Safety and Health, Division of Laboratories and Criteria Development NIOSH Publication No. (NIOSH)75-111, 23 pages (1974).

Concentrations of 250, 500, and 750 ppm vinyl chloride (VC) were passed through 4 types of approved organic vapor respirator cartridges and 4 types of approved front or back mounted organic vapor gas mask canisters until breakthrough occurred. Conventional activated charcoal has a low adsorption capacity for VC. In tests of 50 ppm and 50% humidity, the minimum service life expected was 20 minutes in respirator organic vapor cartridges. Organic vapor front or back mounted gas mask canisters have sufficient life for 100 minutes at concentrations of less than 100 ppm. Neither half-mask organic vapor respirators or full-facepiece gas masks provided adequate protection when considering a no-detectable level of exposure. More efficient sorbents should be developed.

REGULATION; PROTECTION; RESPIRATORY

<226>

Smyth, R.F., Jr., Improved communication--Hygienic standards for daily inhalation., Amer. Ind. Hyg. Assoc. Qtrly. 17(2): 129-185 (see 143, 179) (1956).

This extensive review of inhalation standards presents tabulated toxicity data and very brief summaries on many compounds. A threshold limit of 500 ppm for vinyl chloride was proposed in 1947 on the basis of single animal inhalation studies, and human response. No effect from daily eight-hour inhalations at this level was predicted, and narcosis was the most important effect for ten times the threshold limit. Lung-injuring halogen compounds evolving from vinyl chloride on pyrolysis or contact with hot metal also present a hazard. The recommendation for the standard remained the same in 1956.

STANDARDS; LUNG; OCCUPATIONAL EXPOSURE; REVIEW; DEGRADATION

<227>

Society of Plastics Engineers, Inc.; Palisades Section/Vinyl Plastics Division, VCM, The processors' perspective., Regional Technical Conference, NY, NY Oct. 31-Nov. 1 (1974)

The Society of Plastics Engineers, Inc. held a 2-day Regional technical conference to disseminate information relative to the new standard limiting exposure to vinyl chloride monomer (VCM), and to emphasize its effect on the polyvinyl chloride processor. Sessions were held to establish a perspective on the problem, on the OSHA Standard and its interpretation, on the Environmental Protection Agency viewpoint, on the Food and Drug Administration viewpoint, on analytical devices and methods, and on protective devices and process optimization. Approximately 20 papers were presented.

MANUFACTURE; ANALYSIS; OCCUPATIONAL EXPOSURE

<228>

Spector, W.S., (Ed.), Vinyl chloride, Handbook of Toxicology, Vol. 1. Acute Toxicities of Solids, Liquids and Gases to Laboratory Animals. W.B. Saunders and Co., Phil., PA. Table II: 351-352 (1956).

Vinyl chloride lethal concentration of vinyl chloride for mice is 625-750 mg/liter or 233,000 - 280,000 ppm administered continuously for 10 minutes. Lethal concentration for the guinea pig is 1024 mg/liter or 400,000 ppm administered continuously for 10-20 minutes.

MICE; GUINEA PIG; LETHAL CONCENTRATION (LC)

<229>

Stecher, P.G. (Ed.), Vinyl chloride., The Merck Index: An Encyclopedia of Chemicals and Drugs. Merck & Co., Rahway, N.J. 8th ed., p 1108 (1958).

Chloroethylene (CH<sub>2</sub>=CHCl) is a synonym for vinyl chloride. The gaseous chemical was first prepared by Regnault in 1835. A patent for its preparation by halogenation of ethylene was granted to National Distillers and Chemical Corp. in 1959. The colorless gas liquefies in a freezing mixture. Melting point is -160 degrees C; boiling point is -14 degrees C. Vinyl chloride is soluble in alcohol and polymerizes in light or in the presence of a catalyst. The main uses are in the plastics industry, as a refrigerant, and in organic syntheses. It causes necrosis in high concentrations and frostbite by rapid evaporation if spilled on the skin.

PROPERTIES

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Stein, G.; Juehe, S.; Lange, C.-E.; Veltman, G., Skelettveränderungen bei der sogenannten Vinylchlorid-Krankheit (Skeletal alterations in the so-called vinyl chloride illness.), Roentgen Bl. 26: 350-355 (1973).

Roentgenological examination of 10 patients with so-called vinyl chloride illness confirms the typical osteolysis appearing as bands in the terminal phalanges. Appearance of bandlike osteolysis represents a positive diagnosis for the existence of "vinyl chloride disease".

Ger.

HUMAN; BONE; CASE STUDY; ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE; OSTEOLYSIS

<231>

Stein, G.; Juehe, S.; Lange, C.-E.; Veltman, G., Bandförmige Osteolysen in den Endphalangen des Handskeletts. (Band-like osteolysis of the terminal phalanges of the hands.), Fortschr. Roentgenstr. 118(1): 60-61 (1973).

Two polyvinyl chloride autoclave cleaners exhibited band-like osteolyses of the terminal phalanges of the hands. These specific scleroderma-like changes are reversible. The disease is linked specifically to occupational causes.

Ger.

HUMAN; BONE; RAYNAUD'S PHENOMENON; ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE

<232>

Stender, J., Proposed standard for vinyl chloride., Fed. Register 39(92): 16896-16900 (1974).

On May 6, 1974, the proposed permanent standard for human exposure to vinyl chloride was set at a no detectable level, as determined by methods capable of detecting 1 ppm with an accuracy of 1 ppm plus or minus 50%. This reduced standard resulted from data indicating that 2 of 200 mice exposed to 50 ppm

vinyl chloride 7 hr/day, 5 day/week for 7 months developed angiosarcoma of the liver. Engineering and work practice programs to reduce levels below detectability, as well as respiratory protection programs and protective clothing for workers in regulated areas are required by the standard. Employee training and written operational and emergency plans are to apprise employees of vinyl chloride exposure hazards. Comprehensive medical examinations and tests are proposed. Incidents resulting in the release of vinyl chloride are to be reported to OSHA.

STANDARDS; HUMAN; OCCUPATIONAL EXPOSURE

<233>

Stender, J., Emergency temporary standard for exposure to vinyl chloride., Fed. Register 39(67): 12342-12344 (1974).

A new emergency temporary standard for occupational exposure to vinyl chloride became effective April 5, 1974. The standard applies to any area or operation in which vinyl chloride is manufactured, reacted, handled, processed, released, repacked, or stored. It does not apply to handling, storage or other use of vinyl chloride polymers and copolymers in the form of fabricated products. Maximum permissible exposure is lowered from 500 to 50 ppm, with monitoring by gas chromatography of samples collected by detection devices worn by personnel. All monitoring is to be recorded with records retained for 5 years. Work expected to release vinyl chloride in excess of 50 ppm, such as repair, maintenance, or cleaning of reactors shall require continuous flow or pressure-demand air-supplied respirators or self-contained breathing apparatus. This standard is to be in effect no longer than 6 months, while the safe limits of exposure of humans to vinyl chloride is being determined. These rules and regulations include sections on background, carcinogenicity of VC, petitions for an emergency temporary standard, the standard, and detailed promulgations regarding VC.

STANDARDS; HUMAN; OCCUPATIONAL EXPOSURE; REVIEW; ANGIOSARCOMA

<234>

Stender, J., Standard for exposure to vinyl chloride., Fed. Register 39(194): 35890-35898 (1974).

Effective January 1, 1975, the Department of Labor Standard of Exposure for vinyl chloride will provide that no employee may be exposed to concentrations greater than 1 ppm over any 8-hr period, or to more than 5 ppm averaged over any 15 min period, or to any direct contact with liquid vinyl chloride. "Action level" is defined as 0.5 ppm VC over an 8-hr day. Initial monitoring shall determine exposures in excess of the action level; shall then be repeated monthly if in excess of the permissible exposure limit, or quarterly if in excess of the action level, or at any change which may cause excess of the action level. Regulated areas, limited to authorized personnel recorded on a daily roster, shall be established where VC or PVC is manufactured, reacted, repackaged, stored, handled or used, or where VC concentrations are in excess of the permissible exposure limit. Engineering work practice controls, supplemented where necessary by respiratory protection, and written in plans to be updated every 6 months, shall be used to reduce exposures to the permissible limit. Respiratory protection suitable to the atmospheric concentration of VC shall be supplied by the employer from those jointly approved by the Mining Enforcement and Safety Administration, and the National Institute for Occupational Safety and Health (NIOSH). Entry into unknown concentrations, or concentrations greater than 36,000 ppm, may be made only for life rescue. Employees engaged in hazardous operations shall be provided with proper respiratory protection and clean, dry protective garments. Written operational plans for emergency situations shall be developed for each facility storing, handling, or otherwise using VC as liquid or compressed gas, and

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each employee shall undergo training relating to hazards and precautions of its use. A program of medical surveillance shall be provided without cost to each employee. Entrances and containers shall be informatively labeled as to the hazard within. Monitoring, personnel, and medical records shall be maintained for a period of 30 yrs. Background, findings, discussion, and the detailed rules and regulations are to be found in the Standard.

STANDARDS; OCCUPATIONAL EXPOSURE

<235>

Stulova, E.A., (Characteristics of the state of thermoregulation in chronic vinyl chloride poisoning.), Gig. Tr. Prof. Zabol. 17(3): 53-55 (1973). (BA 57: 23156)

Workers -- 40 men and 56 women from 25 to 45 yrs of age -- exposed chronically to vinyl chloride for 3 to 15 yrs exhibited both subnormal and increased body temperatures. Acrohypothermia, decreased arterial flow, and spasm of capillaries and medium caliber arteries could not be attributed entirely to the state of the peripheral circulation. Clinical physiological analysis indicated that these disturbances, and those of heat production, were due to functional impairment of the hypothalamic brain stem structures. Thermoregulation should be studied for early detection of chronic vinyl chloride poisoning.

Russ.

OCCUPATIONAL EXPOSURE; DIAGNOSTIC; THERMOREGULATION

<236>

Suciu, I.; Drejsan, I.; Valaskai, M., Etude des maladies dues au chlorure de vinyle. (Study of illnesses due to vinyl chloride.), Med. Lavoro 58(4): 261-271 (1967).

Clinical and biochemical findings in 168 workers engaged in the production of polyvinyl chloride allowed clarification of the clinical pattern of the induced diseases by such a substance. Besides the narcotic-type syndrome, symptoms of neurasthenia were observed after repeated exposures. Liver enlargement was present in 30.2% of the cases; Raynaud's syndrome was observed in 6%. Skin manifestations were chemical and allergic dermatitis and scleroderma. In 50% of cases with scleroderma, thyroid impairment was also observed. The skin and muscle biopsy, performed in 3 cases, showed a pattern of collagenosis. All skin manifestations had disappeared within a year after stopping work, except in one case. The initial appearance of nervous manifestations and of digestive, angioneurotic, and cutaneous phenomena suggests that cerebral cortex damage, and later on diencephalic and endocrine damage, play an important role. (modified author abstract)

Fr.; Eng. Sum.

NAPCOSIS; NEUROLOGICAL; LIVER; SKIN; RAYNAUD'S PHENOMENON; EPIDEMIOLOGY; ANGIONEUROSIS

<237>

Suciu, I.; Drejsan, I.; Valaskai, M., Contributii la studiul bolnavirilor produse de clorura de vinil. (Contributions to the study of diseases caused by vinyl chloride.), Med. Interna 15(8): 967-978 (1963).

Toxic symptoms in a group of 168 employees from 2 polyvinyl chloride plants included the narcotic syndrome and angioneurotic disturbances. Hepatomegaly was present in 30.2% of the cases and Raynaud's syndrome in 6%. Cutaneous manifestations consisted of chemical and allergic dermatitis as well as scleroderma. Biopsy revealed collagen disease in 3 cases. All cutaneous manifestations (except in one case) disappeared within one year after interrupting work in the polyvinyl chloride plant. Cortical dynamic disturbances and, later,

the diencephalic centers and endocrine system play a role in causing these symptoms.

Rom.; Eng. Sum.

LIVER; SKIN; GASTROINTESTINAL; NEUROLOGICAL; ANGIONEUROSIS; BIOCHEMISTRY; HUMAN; RAYNAUD'S PHENOMENON; OCCUPATIONAL EXPOSURE

<238>

Suciu, I.; Prodan, L.; Ilea, E.; Paduraru, A.; Pascu, L., Clinical manifestations in vinyl chloride poisoning., Ann. N.Y. Acad. Sci. 246: 53-69 (1975).

In 1961, the study of clinical and biological manifestations in workers of vinyl chloride (VC) manufacturing plants was begun. Examinations were repeated by the same staff from 1962 through 1969. Acute and subacute poisonings occurred with high concentrations of VC, but when concentrations were decreased by 22 times, acute poisonings disappeared and chronic manifestations occurred. Changes in the nervous, cardiovascular, digestive, cutaneous, endocrine, and hematologic systems were recorded and studied. Measures such as heratization, reduction of hours of exposure, vitamin therapy, change in job, and a 22-fold reduction in toxic substance in the air reduced symptoms by two-thirds. The results and discussion section is subdivided into nervous manifestations, cardiovascular manifestations (arterial hypertension), digestive manifestations, respiratory manifestations, cutaneous manifestations, endocrine alterations, hematologic changes, and prophylactic and therapeutic measures.

SKIN; LUNG; CARDIOVASCULAR; NEUROLOGICAL; LIVER; ENDOCRINE; EPIDEMIOLOGY

<239>

Tabershaw, I.R.; Gaffey, W.R., Mortality study of workers in the manufacture of vinyl chloride and its polymers., J. Occup. Med. 16(8): 509-518 (1974).

A mortality study of 8384 men who had at least one year of occupational exposure to vinyl chloride demonstrated that cancers of the digestive system, respiratory system, brain, and cancers of unknown site occurred more often than expected in those workers with the greatest exposure. There was an unexplained inverse relation of buccal cavity and pharynx cancers to exposure. The overall mortality of the study population was approximately 75% of the expected, with no statistically significant cause of death other than that expected in a comparable population. No cases of angiosarcoma of the liver were found which had not been previously identified. There was a consistent pattern of increased mortality from cancer with an increase of exposure or estimated exposure to vinyl chloride.

CANCER; ANGIOSARCOMA; OCCUPATIONAL EXPOSURE; STATISTICS; EPIDEMIOLOGY; MORTALITY

<240>

Takeuchi, Y.; Nabuchi, C., A case of occupational acroosteolysis, presumably caused by vinyl chloride., Jap. J. Ind. Health 15: 385-394 (1973).

Japan is second to the United States in production of vinyl chloride. Raynaud's phenomenon was reported among workers in a vinyl chloride (VC) manufacturing plant in 1954. Three of these workers were reexamined in 1970 but neither Raynaud's phenomenon nor acroosteolysis was found. The case study of a 36-yr old man who had worked as a VC polycleaner for 4 1/2 years revealed acroosteolysis, Raynaud's phenomenon, scleroderma, and induration of both hands. The epidermis of the skin of the left hand was normal, but collagen fibers were edematous, and thickened wall and infarction of vessels was present in the corium. Certain sequelae to the vinyl chloride poisoning persisted after 9 yrs away from the job as polycleaner. Present maximum acceptable concentration of VC in Japan is 500 ppa.

Jap.; Eng. Sum.

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ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON; SKIN;  
OCCUPATIONAL EXPOSURE; HUMAN; CASE STUDY

&lt;241&gt;

Technology Conferences Associates, The vinyl chloride monomer and PVC problem., Conference of El Segundo, California February 27, 1975.

The conference heard reports on 1) Regulatory Concepts for VCM Exposure, 2) EPA Assessment of the Vinyl Chloride and PVC Problems, 3) What SPI is Doing about the Challenge Facing the VCM/PVC Industry, 4) The Enigma of OSHA's VCM Ruling, 5) Measurement and Monitoring of VCM in Plant Atmospheres, 6) Detection and Analysis of VCM, 7) The Use of Respiratory Equipment Against Vinyl Chloride, 8) Economic Aspects and Technical Problems of the PVC Producer and Fabricator, 9) Reduction and Control of VCM in PVC by Advanced Mixing and Compounding Techniques, 10) How Will the Federal Regulations Affect the Supply of PVC, and 11) How do the Federal Regulations Affect the Fabricator and Can He Ensure Compliance?

CONFERENCE

&lt;242&gt;

Thomas, L.B.; Popper, H., Pathology of angiosarcoma of the liver among vinyl chloride-polyvinyl chloride workers., Ann. N.Y. Acad. Sci. 246: 269-277 (1975).

Pathologic materials from a limited number of vinyl chloride-polyvinyl chloride (VC-PVC) workers, some of whom had angiosarcomas of the liver, were reviewed for gross and microscopic features of hepatic angiosarcoma. Based on microscopic observations, a continuous spectrum of changes were manifest initially by multifocal areas of stimulated sinusoidal cells, followed by increasing degrees of sinusoidal cell atypia and proliferation associated with sinusoidal dilatation, culminating in a progressively growing, infiltrative angiosarcoma with a sinusoidal growth pattern. The series of changes appears to be multicentric but only some of the lesions progress to fully developed angiosarcomas. Earliest histologic changes of sinusoidal cell atypia and proliferation which would characterize definite and progressive angiosarcoma were not identified. Whether it was possible to determine by microscopic observation whether angiosarcomas in organs other than the liver represent metastases of primary neoplasms. Proliferation of the hepatocytes apparently influence angiosarcoma development. Histologic features varied considerably in different portions of the angiosarcoma in the same liver and in the angiosarcomas of the liver from different patients, but many features were similar such as sinusoidal, papillary, and cavernous growth patterns coincident with the precursor lesions of proliferation and atypia of sinusoidal lining cells.

ANGIOSARCOMA; LIVER; PATHOLOGY; HISTOLOGY

&lt;243&gt;

Forkelson, T.R.; Oyen, P.; Rove, V.K., The toxicity of vinyl chloride as determined by repeated exposure of laboratory animals., Amer. Ind. Hyg. Assoc. J. 22(5): 354-361 (1961).

Rats showed micropathological changes after repeated, daily 7-hour exposures to vinyl chloride at 500 ppm for 4.5 months. Repeated 7-hour exposures at 200 ppm for six months resulted in liver changes in rabbits and rats, but no detectable changes in dogs and guinea pigs. All species studied tolerated repeated daily 7-hour exposures to 50 ppm for six months with no detectable injury. The available human experience indicates that injury is not likely while operating under a threshold limit value of 500 ppm. A time-weighted average for all exposure however should probably not exceed 50 ppm.

TOXICITY; RAT; RABBIT; DOG; GUINEA PIG; LIVER; LUNG;

HEART; KIDNEY; SPLEEN; TESTES; STANDARDS

&lt;244&gt;

Tribukh, S.L.; Tikhomirova, W.P.; Levina, S.V.; Kozlov, L.A., (Working conditions and measures for their improvement in production and use of vinyl chloride plastics.), Gig. Sanit. No. 10: 38-44 (1969). (CA 44: 1744a)

Chlorinated hydrocarbons in the atmosphere of vinyl chloride production plants average between 0.005 and 0.27 mg/l, with a large proportion of chlorinated biphenyls. In fabrication plants, similar or somewhat higher amounts of chlorine are found. Ventilation needs are stressed. A tendency for respiratory and circulatory disorders, and some cases of hepatitis, were found. Skin eruptions were caused by the chlorinated biphenyl plasticizers. Pressure rolling above 120 to 130 degrees was not recommended.

Russ.

OCCUPATIONAL EXPOSURE; LUNG; CARDIOVASCULAR; SKIN; LIVER

&lt;245&gt;

Turoski, V., The determination of vinyl chloride in aerosol formulations and can linings., Abstracts of Papers, American Chemical Society, 169th National Meeting, April 6-11 (1975) Analytical Section, Abstract No. 122 (1975).

Using two methods of gas-liquid-chromatography, vinyl chloride (VC) standards in tetrahydrofuran were prepared and compared. Stability and analysis time are discussed. Methods given enable the analysis of one-tenth ppm vinyl chloride in pure tetrahydrofuran, and to 3 ppm if interfering substances are present.

ANALYSIS; AEROSOLS

&lt;246&gt;

Ueda, K., (Disturbance of human health by chemical substances - Toxicity of organochlorine compounds.), Nippon Ishikai Zasshi (J. Jap. Med. Assoc.) 69(2): 207-216 (1973). (PESTAB 73: 01170)

Organochlorines are soluble in fats, accumulate in fat tissues and the liver, are damaging to the liver, are narcotic, and produce acne. Metabolic and detoxification mechanisms include the action of glutathione-S-alkyltransferase on alkylhalogen compounds, glucuronate conjugation and excretion of chlorophenolic compounds, and mercapturic acid formation and excretion of partially dechlorinated compounds and those bonded to glutathione compounds. Monomeric vinyl chloride is one of the compounds reviewed.

Jap.

PROPERTIES; BIOCHEMISTRY; LIVER; SKIN; HUMAN

&lt;247&gt;

Van Duuren, B.L., On the possible mechanism of carcinogenic action of vinyl chloride., Ann. N.Y. Acad. Sci. 246: 258-267 (1975).

Relevant information bearing on the possible mechanism of action of the carcinogen vinyl chloride is reviewed. Indirect-acting alkylating carcinogens are related with their direct-acting counterparts. Based on earlier studies, noncovalent binding to serum albumin, microsomal membranes, or other target sites may precede activation to a carcinogenic intermediate. Serum albumin binding may be related to the site of origin of acroosteolysis, a disease associated with exposure to vinyl chloride. Trichloroethylene is structurally similar to vinyl chloride and known information concerning its metabolism in animals and man, suggest an alpha-chloro ether or -onium ion as an important intermediate in its metabolism. It is probably

<247> CONT.  
carcinogenic, particularly to the liver but this remains to be established.

BIOCHEMISTRY; METABOLISM; CARCINOGENICITY

<248>  
Vazin, A.M.; Plokhova, E.I., (Obtaining an experimental model of the toxic angioneurosis arising under the chronic effect of vinyl chloride vapor on the organism.), Gig. Tr. Prof. Zabol. 12: 47-49 (1968).

Rabbits exposed chronically to vapors of vinyl chloride in concentrations of 9 to 10 mg/l showed disturbances in the cardiovascular system. A pathology model based on a description of these functional changes could be useful in the study and experimental therapy of toxic angioneurosis.

Russ.

RABBIT; CARDIOVASCULAR; ANGIONEUROSIS; ANIMAL MODEL; DIAGNOSTIC

<249>  
Vazin, A.M.; Plokhova, E.I., (Changes in the rate of inculcation of conditioned reflexes in rats on prolonged exposure to vinyl chloride vapor in concentrations approaching the maximum permissible concentration.), Gig. Sanit. (Hyg. Sanit.) 35(4/6): 434-435 (1970).

Twenty albino rats (10 experimental, 10 controls) required an average of 10 and 10.4 presentations, respectively, to acquire a stable conditioned reflex to a stimulus (metronome). Latent time required to respond to the stimulus was 4.5 and 4.6 seconds, respectively. After the experimental rats had been exposed to "3-4 vinyl chloride vapor/m<sup>3</sup>" (sic) daily for 4 months in a hermetically sealed 100-liter chamber, 11 presentations of a new stimulus (bell) were required to arrive at a stable conditioned reflex. No increase in latent period of response was detected. It was concluded that prolonged exposure to vinyl chloride in concentrations approaching the maximum permissible concentration may produce alterations in the functional state of the higher divisions of the central nervous system.

RAT; NEUROLOGICAL

<250>  
Vazin, A.M.; Plokhova, E.I., (Changes of cardiac activity in rats chronically exposed to vinyl chloride vapors.), Parazit. Toksikol. 32(2): 220-222 (1969).

Albino rats exposed to vinyl chloride vapors - 0.03 to 0.04 mg/l for 5 months - exhibited cardiac rhythm disturbances, developed bradycardia, and showed reduced I-II and T-II sound intervals without marked changes in the Q-T interval. Cardiac rhythms returned to normal within 15 days after termination of exposure whereas the I-II and T-II intervals continued significantly below the control level for 15-30 days. Resultantly the maximum permissible concentration of vinyl chloride at 0.03 mg/l appears to have been overestimated.

Russ.; Eng. Sum.

TOXICITY; RAT; CARDIOVASCULAR; STANDARDS

<251>  
Vazin, A.M.; Plokhova, E.I., (Changes in adrenaline-like substances in rabbit blood following chronic exposure to vinyl chloride fumes.), Gig. Tr. Prof. Zabol. 13(6): 46-47 (1969).

Chinchilla rabbits were exposed to 0.02 mg to 0.03 mg/l vinyl chloride in air for 4 hours daily over a period of 5 months. After 40 days the level of adrenaline and adrenaline-like substances in the blood stream had risen from 3.5 ug % to 6.6 ug %

where it remained constant. Hypertension was attributed to this effect of vinyl chloride.

Russ.

RABBIT; HYPERTENSION; ADRENAL

<252>  
Vazin, A.M.; Plokhova, E.I., (Pathogenic effect of chronic vinyl chloride exposure to rabbits.), Parazit. Toksikol. 31(3): 369-372 (1968).

Chronic poisoning in rabbits with 9 to 10 mg/l vinyl chloride produced changes in the bioelectric activity of anterior and posterior groups of the hypothalamus nuclei. Cardiovascular changes included alterations in pulse, arterial pressure, and circulation rate.

Russ.; Eng. Sum.

NEUROLOGICAL; CARDIOVASCULAR; RABBIT;

<253>  
Veltman, G.; Lange, C.-Z.; Juebe, S.; Stein, G.; Bachner, U., Clinical manifestations and course of vinyl chloride disease., Ann. N.Y. Acad. Sci. 246: 6-17 (1975).

Seventy patients were examined who had been employed through a range of 6 months to 21 3/4 yrs with an avg of 7.7 yrs, in cleaning polyvinyl chloride (PVC) autoclaves; in centrifuging, drying, and sifting processes in PVC manufacture; and with wrapping PVC as an end product. Initial symptoms included upper abdominal complaints (in 60% of the cases), tiredness, dizziness, numbness in fingers and toes, increased perspiration, cold fingers or hands, arthralgia, impotency, and head- and leg-aches. Outstanding objective symptoms were thrombocytopenia in 81%, increased BSP retention in 67%, splenomegaly in 57%, and reticulocytosis in 41%. Skin changes consisted of club-like swelling and shortening of the fingers, and coarse white to ivory-colored infiltrates ranging from grains to small nodules. Histologically there was hyperorthokeratosis and thinning of the epidermis, endothelial swelling and lymphocytic infiltrate in the subepidermal boundary layer, and swollen or homogenous collagen bundles, with the elastic fibers showing evidence of rarefaction, fissuration, and fragmentation. No direct correlation was found between these findings and the severity of internal findings. Vascular changes ranged from slight narrowing of the vascular lumina to complete absence of filling of the arteries along the whole length of the finger. Slight to severe thrombocytopenia was found with such frequency as to make the platelet count an obligatory test in all PVC workers. Improvement of platelet count was observed in only 6 of 29 patients in 1 to 1 1/2 yrs after quitting their jobs. Improvement in skin and bone changes was more frequent.

ACROOSTEOLYSIS; SKIN; BONE; THROMBOCYTOPENIA; OCCUPATIONAL EXPOSURE; HUMAN; CARDIOVASCULAR; CASE STUDY

<254>  
Viola, P.L., Carcinogenic effect of vinyl chloride., Abstracts. Tenth Int. Cancer Conf., Houston, Texas Session 56: 742 Abstract No. 29 (1970).

Male Wistar rats, weighing 150 g, were exposed to 3 vol % vinyl chloride at the rate of 4 hr/day, 5 days/week, for 12 months. After 10 months, 70 percent developed squamous cell carcinoma of the external auditory meatus. Thirty-two percent developed carcinomas and adenocarcinomas showing typical signs of squamous metaplasia in the lungs. Twenty-five percent showed chondroid metaplasia of bone tissue with intense periosteosis particularly located in the tarsal and metatarsal bones.

CANCER; RAT; LUNG; BONE; EAR

<255>

Viola, P.L., Pathology of vinyl chloride., Med. Lavoro 61(3): 174-180 (1970).

Twenty-five rats were exposed to vinyl chloride (VC), 3% by weight or 30,000 ppm, 4 hrs/day, 5 days/week for 12 months. The animals were soporific at first; at 10 months some showed decreases in weight, in aggressiveness, in reaction to external stimuli, and often disturbed equilibrium. Thirteen died from cardio-respiratory complications, 2 from hemoperitoneum. Most showed brain, liver, kidney, and thyroid degenerative changes; 6 showed histopathological alterations of bones similar to acroosteolysis in man, with periosteal proliferation and chondrial metaplasia. The connective tissue was dissociated; elastic reticulum was reduced and fragmentary; walls of the derma vessels were hypertrophied with lumen sometimes obliterated; and nerve endings were surrounded and infiltrated by fibrous tissue. Reduction of the threshold limit value for VC, and elimination of manual cleaning of autoclaves were recommended.

STANDARDS: RAT; BONE; LUNG; BRAIN; LIVER; KIDNEY; THYROID; ACROOSTEOLYSIS

<256>

Viola, P.L.; Bigotti, A.; Caputo, A., Oncogenic response of rat skin, lungs, and bones to vinyl chloride., Cancer Res. 31: 516-522 (1971).

Rats (AR/1PE Wistar strain) were exposed to a constant flow of air containing 3% v/v vinyl chloride monomer for 12 months, 4 hours a day, 5 days a week. The cutaneous system proved most susceptible to oncogenic effects, with epidermoid carcinomas located preferentially in the area of subaxillary and parotid glands. Tumors also developed in the lungs and bones. Other effects were noted in brain, liver, kidneys and intestinal mucosa. The role of mucus-producing cells is conjectured.

CANCER; SKIN; LUNG; BONE; RAT

<257>

Von Oettingen, V.F., Halogenated olefinic hydrocarbons. Vinyl chloride., The Halogenated Aliphatic, Olefinic, Cyclic, Aromatic, and Aliphatic-Aromatic Hydrocarbons Including the Halogenated Insecticides, Their Toxicity and Potential Dangers, Department of Health, Education and Welfare PHS Pub. No. 414: 195-197 (1955).

This comprehensive 1955 review of hydrocarbons surveys the literature concerning the toxicity of vinyl chloride to humans and to test animals from 1930 (Patty, Yant, and Waite) through 1947 (Oster, Carr, Krantz, and Sauerswald), and notes that the American Conference of Government Industrial Hygienists accepted 200 ppm as the Threshold Limit for continued exposure in 1953.

REVIEW; STANDARDS

<258>

Wagner, E.R.; Muellder, W.W., A procedure for preparing 14C-labeled vinyl chloride., Ann. N.Y. Acad. Sci. 246: 152-153 (1975).

To prepare the labeled vinyl chloride, 1,2-dichloroethane-1,2-14C was injected into an 8 foot x 1/4 inch diameter U-shaped glass chromatographic column, packed with 80-90 mesh 25X Dow Corning 410 Gum on acid-washed Chromosorb W except for the top 35 cm, packed with a catalyst prepared by mixing 20 g of Chromosorb W and 10 g of Darco G-60 charcoal. The catalyst portion of the chromatograph was heated to 440-450 degree C, but the remainder of the column was held at 150 degree C. The second peak (retention time: 1.4 min) was 75-85% of the product mass and was shown to be vinyl chloride by infrared and gas chromatographic analysis.

LABELING; SYNTHESIS

<259>

Weichardt, R., Die Hautgefahrung in der Kunststoffindustrie. (Endangering the skin in the plastics industry.), Berufsdermatosen 18(1): 25-34 (1970).

Toxic substances used without appropriate protective measures are particularly dangerous in the plastics industry. A review of the literature on skin lesions produced by synthetic materials includes epidemiological studies in Japanese and English polyvinyl chloride industries.

GER.; ENG. SUM.

REVIEW; ACROOSTEOLYSIS; RAYNAUD'S PHENOMENON; SKIN; BONE; EPIDEMIOLOGY; CASE REPORT

<260>

Weinberg, J.H., Toxic surprises from the plastics industry., Sci. News 106(10): 154-155, 157 (1974).

Two and one-half million workers produce more than 29 billion pounds of plastics yearly in the United States. Many plastic components are toxic. Fifteen vinyl chloride workers died this year reportedly from liver cancer which was chemically induced. Small, still undefined amounts of vinyl chloride cause fibrotic lesions on the liver after only a year or so of exposure. Unpolymerized vinyl chloride is metabolized to monochloroethylene oxide, the probable carcinogen that acts upon liver cell membranes. It is more damaging in fasting animals, probably because of depletion of a membrane protective substance. Current regulation of the plastics industry is fractionated. The Toxic Substances Control Act passed by both houses of Congress is now in conference committee. Much data needed for setting effective standards lies within industry. There is consensus on need for research on new and existing components of plastics.

STANDARDS; OCCUPATIONAL EXPOSURE; CANCER; ANGIOSARCOMA

<261>

Wilson, R.H.; McCorsick, W.E.; Tatus, C.F.; Creech, J.L., Occupational acroosteolysis., JAMA 201(8): 577-581 (1967).

Among 3,000 personnel involved in vinyl chloride manufacturing and polymerization, 31 cases of hand acroosteolysis were diagnosed--particularly osteolysis specific to the distal phalanges of hands. Raynaud's symptoms were associated frequently with this disorder. This condition results primarily from three conditions: 1) a chemical insult, 2) a physical insult, and 3) a personal idiosyncrasy. Twenty-seven of the 31 men had a positive correlation to the "polycleaner" job assignment.

ACROOSTEOLYSIS; OCCUPATIONAL EXPOSURE; RAYNAUD'S PHENOMENON; SKIN; BONE; CASE STUDY; HUMAN; EPIDEMIOLOGY; POLYCLEANER

<262>

Vithey, R.J., Uptake and pharmacodynamics of vinyl chloride administered to rats by different routes., Abstracts of Papers for 14th Annual Meeting of Society of Toxicology, Williamsburg, Virginia, March 9-13 (1975) Abstract No. 60: p. 49 (1975).

To assess the hazard presented by the oral ingestion of vinyl chloride monomer, rats -- surgically prepared with an indwelling jugular cannula -- were dosed by intragastric intubation with solutions containing up to 2 mg/ml of aqueous vinyl chloride; sequential samples of blood allowed time concentration curves to be obtained. Uptake of vinyl chloride by this route is extremely rapid, peak concentrations being achieved less than 10 min after administration. Elimination from the blood

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compartment appears to be biexponential, the slower terminal phase having a half-life of about 6 min. Studies with the same animal model, in a single restraint cage, exposed to concentrations of vinyl chloride of up to 2000 ppm in the gas phase have shown a similar rapid uptake followed by a plateau blood concentration during several hours of exposure. On removal from the vinyl chloride atmosphere, blood concentrations fall rapidly to barely detectable concentrations after 30 min.

BIOCHEMISTRY; RAT; INGESTION

<263>

Wolf, P.; Kreter, B., Zur Diffusion von monomeren Vinylchlorid in Polyvinylchlorid. (Diffusion of vinyl chloride monomer in polyvinyl chloride.), Plaste Kaut. 21(1): 27 (1974). (CA 80: 146581P)

The diffusion coefficient of vinyl chloride in polyvinyl chloride was inversely proportional to the K-value, probably as a result of greater chain mobility. Diffusion was lower at 50 degrees than at 20 degrees, and attainment of equilibrium was slower at 50 degrees. Neither particle size nor plasticization time systematically affected the diffusion.

G.F.

PROPERTIES

<264>

Wyatt, R.H.; Kotchen, J.N.; Hochstrasser, D.L.; Buchanan, J.W., Jr.; Campbell, D.B.; Slaughter, J.C.; Doll, A.H., An epidemiologic study of blood screening tests and illness histories among chemical workers involved in the manufacture of polyvinyl chloride., Ann. N.Y. Acad. Sci. 246: 80-87 (1975).

An epidemiological comparison of workers in the polyvinyl chloride (PVC) production unit with workers in other parts of the Louisville B.F. Goodrich plant was undertaken in order to discern any detectable blood screening test or illness history differences between the two groups. Employment and medical histories were obtained from company records. Allergic problems and liver-spleen disease were reported more frequently in the PVC production workers, but genitourinary illnesses were more frequent in the other group of workers. Twelve blood screening tests were administered. The production workers had a greater percentage of abnormal albumin levels, while the control group had a greater percentage of clinically elevated SGOT and alkaline phosphatase levels. The effect of age on cholesterol levels was significantly different for the two groups.

EPIDEMIOLOGY; OCCUPATIONAL EXPOSURE; BLOOD; DIAGNOSTIC

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