physical examinations failed to reveal any chronic effects from long-term exposures to vinyl acetate at the time-weighted levels of from 5 to 10 ppm. No eye or upper respiratory irritation was noted below 10 ppm but were definite at 21 ppm. The present threshold limit value for vinyl acetate is 10 ppm.

TOXICOLOGY OF VINYL CHLORIDE

The earliest studies on vinyl chloride were limited to *acute exposures*. These observations led to its consideration as a surgical anesthetic. About 20–25 years ago, during the earlier work exposures, the chief concern was to keep workroom atmospheric concentrations below the explosive limit (3½% or about 30,000 ppm); men commonly worked at exposure levels of 3000–4000 ppm (near the narcosis level), and it was not at all unusual to have men leave the work place for relief and fresh air outside. Generally, these studies showed vinyl chloride to be low in acute toxicity, to be anesthetic in action and to have little capacity to cause liver injury from exposures of a few hours. Mastromateo *et al.*[35] and Lester *et al.*[37] reported on acute exposures of animals and humans. They reported very little effect until exposure concentrations approached 10,000 ppm, when humans reported dizziness after 5 minutes' exposure.

Torkelson *et al.*[48] conducted animal studies to determine chronic toxicity to assess the hazards to humans. Vinyl chloride was found to have a slight capacity to cause liver and kidney injury on repeated exposures. Male and female rats showed micropathologic changes after repeated 7-hour exposures at 500 ppm for 4.5 months. Repeated 7-hour exposures at 200 ppm for 6 months resulted in micropathologic changes in the livers of rabbits and statistically significant increases in the average weight of the livers of male and female rats but no detectable changes in dogs and guinea pigs. Repeated 7-hour exposures at 100 ppm resulted in slight increases in the average weight of rat livers; the other species were not affected. All species studied tolerated repeated daily 7-hour exposures to 50 ppm for 6 months with no detectable injury.

Repeated daily 1-hour exposures at 200 and 100 ppm of vinyl chloride were without effect; longer exposures caused a slight increase in liver weight.

The standard for evaluating regular daily 7–8-hour exposures may be defined as the concentration below which practically all analytic results must fall. The value of 100 ppm was suggested as the standard for vinyl chloride, with a time-weighted average for all exposures not to exceed 50 ppm (Torkelson, *et al.*[48]).

Lester *et al.*[37] differed with the conclusions of Torkelson *et al.*[48] and recommended 500 ppm as a time-weighted average exposure.

Because of these conflicting reports, the TLV Committee of the ACGIH[2] in 1963 chose to change their TLV from 500 ppm as a maximal time-weighted average for industrial exposure to 500 ppm as a ceiling value.

Harris and Adam[20] studied workers engaged in the polymerization of vinyl chloride, reporting 2 cases in which autoclave cleaners in the vinyl chloride polymerization process were scraping the walls of the autoclave to remove the polyvinyl chloride with considerable hand/skin contact. Acroosteolysis was reported to have occurred in 2 workers.

Of the 588 polyvinyl chloride workers in this plant, including 150 autoclave cleaners, 2 cases were identified based on x-rays of the hands of these workers. The terminal phalanges of the hands, the patella and the phalanges of the feet were involved. Two other workers, also autoclave cleaners, demonstrated early

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changes accompanied by Raynaud's phenomenon.

Wilson *et al*[52] studied 31 cases of occupational acroosteolysis of the hands of workers engaged in vinyl chloride polymerization processes, and most of these had worked as cleaners of vessel walls and other equipment in the polymer process. The acroosteolysis was localized to the distal phalanges of hands and frequently was associated with Raynaud symptoms. They reported the disorder to have resulted from a combination of physical insult, chemical insult and personal idiosyncrasy and were unable to name specific causes. Prevalence was reported to be less than 3% among employees performing similar work, and no cases were found in workmen processing the polymer or manufacturing commercial resins. More than 100 workers handled the finished resin; those who processed it into plastic products did not demonstrate findings of acroosteolysis.

In 1970 and 1971, the Institute of Environmental and Industrial Health at The University of Michigan[13] conducted a comprehensive study of acroosteolysis in workers producing and compounding vinyl and polyvinyl chloride. The epidemiologic population represented more than 5000 workers in 32 plants. Thirty-one cases were discovered, of which 25 had a definite diagnosis; there were 16 suspicious diagnoses of acroosteolysis clearly associated with hand cleaning of the polymerizers.

Dodson and co-workers[14] determined that work practices rather than any specific agent or combination of agents appeared to relate to the occurrence of the disease. These investigators thought the disease to be of systemic rather than localized nature, but were unable to define the etiologic agent or portal of entry, suggesting some idiosyncratic "sensitization of susceptibility." An industrial hygiene survey of this epidemiologic investigation[9] revealed vinyl chloride concentrations in the reactor before ventilating to be about 3000 ppm. After aeration of the containers, the vinyl chloride concentra

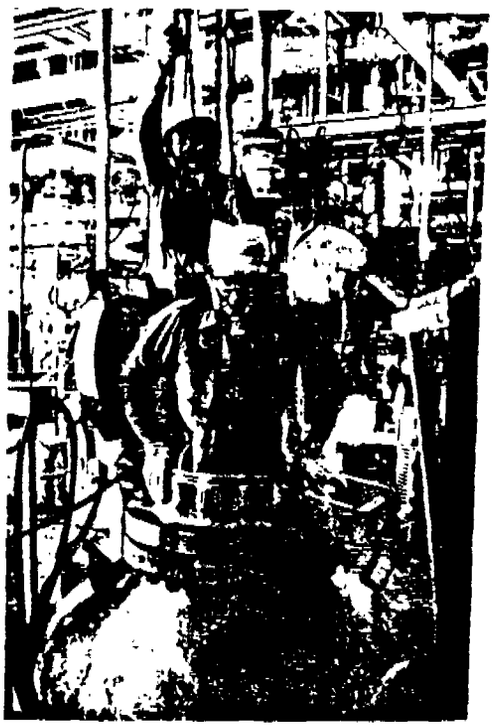

Fig. 31–2.—A worker entering a polyvinyl chloride reactor vessel to clean out caked polymer adhering to the inner surfaces. During the polymerization reaction, sludge from the slurry has a tendency to form a crust on the impeller mechanism as well as the tank inner surfaces. The caked polymer is periodically hand-chipped by workers inside the tank, and this is the operation that subjected workers to the highest concentrations of vinyl chloride. Current practice requires that flexible ducts be used for purging with clean air before the worker enters. In addition, workers in this operation must be provided with positive-pressure air-supplied respirators preferably the hood type. Demand-type respirators have been used, but may not offer the same protection as the continuous-flow type of hood respirator. (Courtesy of Maurice N. Johnson, M.D., B. F. Goodrich Company, Akron, Ohio. Photographer—H. Groskinski.)

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Fig. 31–3.—The solid, caked polymer must be removed by chisels, hammers and handpicks. Neither workers nor management may be aware of the hazard involved when a spark is generated by steel on steel. It is not uncommon to open a pocket of the cake lining the vessel. The pocket may contain liquid vinyl chloride monomer. It is very possible that the lower explosive limit for vinyl chloride monomer (33,000 ppm) can be reached during the chipping with steel on steel. Reactor vessels have exploded, leaving nothing but a crater in the ground where the plant once stood. Reactor chipping or cleaning tools should be of the nonsparking type. To minimize worker entry, some companies use high-pressure water guns to remove the caked polymer. These water guns may operate from 9000 to 13,000 pounds of pressure per square inch. This in itself may produce a serious safety hazard. Some attempts in the United States to remove the caked slurry have utilized closed solvent cleaning systems in which solvents such as tetrahydrofuran are used. To date, such solvent cleaning systems have been relatively unsuccessful. Recently completed production systems using 30,000-gallon reactor vessels have been utilizing automatic high-pressure water cleaning guns and solvent systems to minimize or eliminate the need for worker entry into reactor vessels. Older reactor vessels, which contain cooling vanes of heat exchangers, complicate the cleaning process and high-pressure water guns and solvent systems cannot be used in these tanks. (Courtesy of Maurice N. Johnson, M.D., B. F. Goodrich Company, Akron, Ohio. Photographer—H. Groskinski.)

tion inside the reactors during scraping was found to be under 100 ppm and usually around 50 ppm. It was found that scraping released some unpolymerized vinyl chloride so that *levels of 600–1000 ppm* were *found close* to the *hands* during these operations.* Other possible constituents of the scrapings of the reactor vessels were thought to be polymerized resins, unreacted catalysts, additives and, of course, the polymerized vinyl chloride. No serious disability had been reported in any of the above-mentioned cases but a few men had been partially disabled because of hand soreness, with some restriction in manual activity. With proper protective equipment and careful hygienic measures, all these cases are preventable. Vinyl chloride, although thought to be relatively nontoxic and even innocuous, typified by the 1973 threshold limit value of 500 ppm and known mainly as a narcotizing substance when inhaled in high concentrations, recently has caused alarm in occupational health practitioners. Conjunctivitis, corneal burns and dermatitis have been seen, and high concentrations and prolonged exposures cause headaches, dizziness and some irritation of the upper respiratory tract. With extreme exposures, narcosis may occur, and it has been apparent from the acroosteolysis reports mentioned that preventive measures were undertaken lightly.

*Our italics, implying the potentially high worker respiratory inhalation.

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Because of the report of acroosteolysis in humans, Viola[50] attempted to produce the disease in animals. He exposed rats 4 hours per day, 5 days per week to 30,000 ppm (3%) vinyl chloride vapor. In his first report on the results of 12 months' exposure, he described metaplastic changes in the bones, which he considered similar to human acroosteolysis. He made no mention of having observed cancer in these animals until the Tenth International Cancer Congress in May, 1970. In the abstracts of this meeting, and subsequently in May, 1971, Viola *et al.*[51] reported tumors of the skin, lungs and bones occurring first after 10 months' exposure, appearing to be the earliest and only publication in which carcinogenic activity had been ascribed to vinyl chloride.

Observing workers of a PVC-producing plant (Germany), Marsteller *et al.*[34] found esophageal varicosities, splenomegaly and nonspecific liver damage. These observations, together with the abovementioned reports on "subclinical liver damage" initiated an investigation of the pathology of these changes.

Radiologic, biochemical and enzymatic tests, liver scanning, laparoscopy and liver needle biopsy were used in 20 workers (ages 30–56 years) of a PVC-producing plant; length of work exposure was 1½–21 years.

There was a total of 120 workers involved in the production of PVC; 45 of them had been examined at the Department of Dermatology, some because of manifest skin changes, but many were given a preventive examination. In most of these 45 workers, the examination resulted in a clinical and/or biochemical suspicion of liver damage.

Until May, 1973, it was possible to perform laparoscopy in 20 of these 45 workers suspected of having liver damage. The prevalence of liver damage in workers exposed in the PVC-producing plants could not be evaluated on this basis only.

In 13 of 20 cases, the liver was found to be enlarged. Two patients had pain on abdominal palpation in the right upper quadrant; hyperlipidemia had been diagnosed in 1967 (after 6 years of exposure) in another patient, together with "liver damage."

There was a history of jaundice in only 1 patient in 1955, before the onset of exposure; in 1968, a diagnosis of chronic liver dysfunction had been established. There was no history of alcoholism. Splenomegaly was found in 7 of 20 cases (range 1.5–5 cm). Bilirubin (total) exceeded the upper normal limit of 1 mg/100 ml in 3 cases (range 1.1–1.7 mg/100 ml). The bromsulphalein test was abnormal (5% after 45 minutes in 19 cases [range 6.1–21.5]). SGOT exceeded the upper normal limit of 12 mU/ml in 17 cases; in 14 cases, SGPT was elevated (range 15–30). An increased level of alkaline phosphatase was found in 2 patients (48 mU/ml). Hypothrombocythemia (less than $150 \times 10^3/mm^3$) was found in 19 of 20 patients, at least initially, in 12, the initial level was lower than $100 \times 10^3/mm^3$. Acroosteolysis was present in 4 patients. BSR, CBC, glycemia, urinalysis, LDH, cholinesterase, acid phosphatase, iron and copper serum levels, proteinemia and electrophoretic separation of serum proteins, cholesterol, betalipoproteins, triglycerides and plasmatic coagulation factors were not found to be abnormal.

In 3 cases, varicose esophageal veins (and in 2 cases also of the gastric fundus) were visualized.

Laparoscopy showed the following changes: capsular fibrosis in 15 cases, reorganization of the liver architecture in 8 cases, splenomegaly in 7 cases, portal hypertension in 2 cases and hepatomegaly in 4 cases.

The histologic changes encompassed the following: centrilobular collagen

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transformation of the walls of sinusoids in 5 cases, focal activation of Kupffer cells in 9 cases, fatty infiltration (focal) in 14 cases, increased collagen deposition in the portal spaces and portal fibrosis, septal fibrosis or intralobular fibrosis in 17 cases, isolated cellular necrosis in a few cases and a low degree of cholestasis in a few instances.

The biochemical changes and the histologic abnormalities were, in most cases, of a low or moderate degree. The similar findings in many cases, all exposed to the same toxic environment, gave more weight to the above-mentioned observations. In workers at PVC-producing plants, thrombocytopenia, chronic toxic liver damage, with splenomegaly and signs of portal hypertension in some of the cases, are more frequent than acroosteolysis.

In January, 1974, a manufacturer of polyvinyl chloride and copolymers notified its employees, the National Institute for Occupational Safety and Health, the Kentucky State Department of Labor and the public that 3 workers had died of angiosarcoma of the liver. These cases had a common denominator—employment in the manufacture of polyvinyl chloride resins. This report by Creech and Johnson[11] has resulted in an enlarged scope of knowledge and eventually uncovered a total of 14 known angiosarcomas connected with vinyl chloride exposures, all within a few months, from other work places.

Two case reports were described by Creech and Johnson. One of these was reported as: *Patient One*, a 36-year-old white male, was hospitalized January 5, 1970, because of tarry stools. Occupational History: The patient had been employed from November, 1955, until his illness, except for two lay offs of 9 months in 1958 and 6 months in 1959, as a chemical helper and operator in the Louisville plant of a chemical company in the manufacture of polyvinyl chloride resins. Present Illness: At the time of admission, the patient had no complaints except passage of tarry stools. Past history was negative except for an operation for hemorrhoids 4 years earlier. Physical examination showed pallor and black stool on rectal examination. Liver and spleen were not palpable. Although an upper GI series was interpreted as normal, a tentative diagnosis of bleeding duodenal ulcer was made.

On diet and medication, the patient had no recurrence of overt bleeding until May 1, 1970, 4 months later, when he was readmitted for tarry stools. Again, he was found to have marked pallor and tarry stool on rectal examination. At this time, the liver was demonstrably enlarged and the spleen was palpable. Blood chemistry studies ("SMA/12") were not significantly abnormal; total bilirubin, alkaline phosphatase, LDH and SGOT were only slightly elevated. GI series showed only anterior displacement of the stomach, but barium swallow suggested esophageal varices. Intravenous pyelogram was normal; barium enema was normal except for displacement of the splenic flexure by an enlarged spleen. Liver scan on May 4, 1970 was interpreted as being compatible with a large lesion in the left lobe of the liver, extending into the right lobe.

The report of pathologic findings was "liver, biopsy of, angiosarcoma (malignant hemangioendothelioma)." The patient succumbed to the liver tumor on September 27, 1971, 14 months postoperatively, despite cobalt therapy and interarterial infusions of 5 FU.

The authors refer to Viola *et al.*,[51] who had reported in 1971 the oncogenic properties based on experimental use of monomer vinyl chloride. Viola and co-workers performed experiments with pure vinyl chloride on 3-month-old male (albino) rats exposed to vinyl chloride

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vapors for 4 hours a day, 5 days a week for 12 months. The animals were kept in airtight cages in which a constant flow of air containing 3% (equal to 30,000 ppm) of vinyl chloride was passed through. They described the lesions found in the experimental animals and demonstrated that almost all of the animals developed tumors of the skin and lungs, skin tumors most frequently accounting for 65–70%.

Maltoni[29] presented his results of unpublished experiments with vinyl chloride in February, 1974, at a U. S. Department of Labor hearing in Washington, D. C. He has observed liver cancer in rats exposed 4 hours a day, 5 days a week to 250 ppm of vinyl chloride for up to 12 months. An investigation under the auspices of the Manufacturing Chemists' Association[23] reported the development of angiosarcoma in mice after 7 months of exposure to 50 ppm 7 hours a day, 5 days a week.

Mancuso[32] testified that although the focus now is on the experimental cancer-causing effect, it is very important to note that other pathologic changes occur in the brain (degeneration of the nerve cells–cerebellum), severe chronic hepatitis (as well as cirrhosis), interstitial pneumonia and damage to the kidneys. Further, the skin tumors frequently developed near the ear and submaxillary or the same areas as the salivary glands. It was postulated by the investigators that vinyl chloride may enter the salivary gland system. If this is confirmed subsequently, it will raise the question whether tumors of the parotid gland can also occur (as has been demonstrated in the rubber industry). (At this writing there have been 31 cases of angiosarcoma of the liver reported associated with vinyl chloride exposures.) Investigators observing and conducting epidemiologic studies of vinyl chloride monomer workers must be aware of other unusual or unique pathologic findings, such as laryngopharyngeal involvement. These cases have been noted in plants in different locations in the United States and as yet have not been officially reported; however, they reinforce the need to correlate pathologic changes in other organ systems with chronic work exposure.

Analytic Methods

Four methods are available for environmental monitoring of air for the presence of vinyl chloride: combustion-conductivity, gas chromatography, infrared spectrophotometry and flame ionization spectrophotometry. Gas chromatography is very specific but requires about 10 minutes per sample. Flame ionization detectors have no specificity–responding to all carbon-carbon or carbon-hydrogen bonds–but are portable and the measurement is instantaneous. Infrared analyzers are very specific, respond quickly and are portable. All these techniques have adequate sensitivity, detecting concentrations of 1 ppm or less.

Worker monitoring is achieved through the use of absorption tubes filled with activated carbon, and the absorbed chlorinated hydrocarbons are determined by gas chromatography.

Most environmental monitoring has been with combustion-conductivity analyzers. These analyzers are used for continuous monitoring with excellent results. NIOSH recommends the gas chromatographic method with known sensitivity of 1 ppm.

Medical and Hygienic Controls

The National Institute for Occupational Safety and Health[39] published detailed medical and hygienic recommendations for the manufacture and processing of polymer from vinyl chloride on March 11, 1974:

"Consultants from industry who worked with NIOSH proposed that the

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recommended standard contain the concept of an allowable 'working level' for vinyl chloride gas in the atmosphere, which they identified as a time-weighted average of 50 ppm. They recommended that where workers were exposed to concentrations in excess of this level they should wear air-supplied respirators. This concept of an allowable 'working level' might seem justifiable in that Professor Maltoni[29] found no liver tumors at 50 ppm, but there is the possibility that tumors might have been produced if a larger number of animals had been exposed at that concentration. Based on theoretical considerations, there is probably no threshold for carcinogenesis although it is possible that with very low concentrations, the latency period might be extended beyond the life expectancy. In view of these considerations and NIOSH's inability to describe a safe exposure level as required in section 20(a)(3) of the Occupational Safety and Health Act, the concept of a threshold limit for vinyl chloride gas in the atmosphere was rejected.

"Consequently, the recommendations are such that where any employee is exposed to measurable concentrations of vinyl chloride, as determined by the recommended sampling and analytical method, he shall wear an air-supplied respirator. This recommendation is based on some preliminary information that the standard chemical cartridge respirators are inefficient in protecting against vinyl chloride. NIOSH is implementing a study to evaluate the degree of protection afforded by different types of respirators using vinyl chloride as the test gas. As information becomes available, it will be forwarded to OSHA as recommendations for alternative respirator usage. The employer is also required to develop a Control Plan to reduce airborne concentrations of vinyl chloride to levels not detectable by the recommended method."

Similar recommendations have been made for other toxic substances by the ACGIH: "Recommendations for worker exposure by all routes should be reduced to a minimum in the light of the warning of the potency of the substances to induce tumors in animals. 'Reduced to a minimum' means extraordinary care shall be taken both in manufacture and in handling so that worker exposure by all routes is kept below the limit of sensitivity of the analytic method of determining the exposure concentration."[3]

NIOSH Recommendations for Medical Surveillance

The following recommendations are directed primarily at medical screening to detect liver disease and/or hepatic tumor. They should be considered in the context of routine health screening for any general employee health problems, including nonhepatic health conditions potentially related to vinyl chloride monomer exposure. Routine health screening should include at the time of initial employment the recording of past medical history and the performance both of a general physical examination and certain basic laboratory procedures (e.g., complete blood count, urinalysis, chest x-ray); provisions should also be made for routine periodic health follow-up examinations.

Employees covered by the following specific recommendations shall encompass all persons engaged in vinyl chloride monomer production and polymerization, including personnel peripherally involved, such as in clerical and management assignments. The recommendations shall be applied both as a pre-employment requirement and as part of a periodic health follow-up. Screening priority should be given to current employees with prolonged and close potential exposure to vinyl chloride monomer, whether in present or past work settings.

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1. At the time of initial employment, or on institution of screening, a physical examination shall be performed with specific attention to detecting enlargement of liver or spleen by abdominal palpation.

2. At the time of initial employment, or on institution of screening and annually thereafter, a medical history check list shall be completed by the employee. This list shall include questions concerning alcohol intake; past history of hepatitis; past exposure to potential hepatotoxic agents, including drugs and chemicals; past history of blood transfusions; and past history of hospitalizations. The completed medical check list shall be reviewed by a physician and should be acted on as medically indicated for each individual employee.

3. At the time of initial employment, or on institution of screening, a serum specimen shall be obtained for screening with respect to the following 5 biochemical determinations of liver function: total bilirubin, alkaline phosphatase, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and gamma glutamyl transpeptidase (GGTP, if test is available).

Additional tests that may optionally be considered for use in screening include lactic dehydrogenase (LDH), serum protein determinations, serum protein electrophoresis and platelet count. Laboratory analysis shall be performed in laboratories accredited by the College of American Pathologists or licensed in accordance with the provisions of the Clinical Laboratories Improvement Act of 1967.

4. If the results of laboratory screening are normal, screening shall be repeated on an annual basis. If the person being screened has been employed directly in vinyl chloride monomer production or polymerization for 10 years or longer, screening shall be repeated every 6 months.

5. If one or more liver function tests are abnormal, serum testing shall be repeated as soon as possible, preferably within 2–4 weeks. If no abnormalities are present on rescreening, testing should be repeated in 3 months.

6. If abnormalities persist on rescreening, the employee shall be removed from contact with vinyl chloride monomer operations and an individualized medical work-up shall be instituted. Suggested as initial steps in the medical work-up are a complete physical examination and various special procedures, such as hepatitis B antigen determination and liver scanning.

If liver function abnormalities are determined to be unrelated to liver disease (e.g., elevated alkaline phosphatase in a young, physically active man or elevated bilirubin in Gilbert's syndrome) or to be transient (e.g., due to recent hepatitis or recent alcohol intake), the employee may be permitted to return to vinyl chloride-related employment, subject to individual medical evaluation.

7. In view of the preliminary results of animal toxicology studies, it is recommended that no woman who is pregnant or who expects to become pregnant should be employed directly in vinyl chloride monomer operations. [See chapter 30, Lead, by Hernberg, on women of reproductive age who are exposed to toxic threshold limits.]

In summary, these new regulations state that until exposures to vinyl chloride are reduced below detectable levels, employees entering any regulated area shall be provided with and required to wear and use a full-face supplied-air respirator with a continuous flow or a pressure-demand type. In addition, employees are to be provided with and required to wear clean full-body protective clothing and gloves prior to entering the regulated area.

At the Second International Symposium on Cancer Detection and Preven-

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tion, Maltoni[30] concluded his presentation on Occupational Carcinogenesis by stating, "We may diagnose some tumors quite early, but on the basis of 15 years' experience with periodic checks of workers exposed to high risk, I doubt that periodic medical examination has a real bearing in saving people with occupational cancer although detected early, or in prolonging their life span. Thus, my position is in sharp contrast with those who claim to 'protect' (!) workers exposed to carcinogenic risk with medical examinations. I do believe that the potentialities of medical examinations should be evaluated at an international level. In conclusion, I would like to emphasize the need for a close collaboration among scientists, public health services, workers' unions and industries, to evaluate the risks and to devise preventive measures for avoiding or minimizing occupational tumors."

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REFERENCES

1. American Conference of Governmental Industrial Hygienists: Proceedings of the 28th Annual Meeting, Pittsburgh, May, 1955.
2. American Conference of Governmental Industrial Hygienists: TLV for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1963, Cincinnati, Ohio.
3. American Conference of Governmental Industrial Hygienists: TLV for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1973, p. 41, Cincinnati, Ohio.
4. American Conference of Governmental Industrial Hygienists: TLV for Chemical Substances and Physical Agents in Workroom Environment with Intended Changes for 1974, Cincinnati, Ohio.
5. Block, J. B.: Angiosarcoma of the liver following vinyl chloride exposures, JAMA 229:53, 1974.
6. Bourne, H. G., Yee, H. T., and Seferian, S.: The toxicity of rubber additives, Arch Environ. Health 16:700, 1968.
7. Brieger, H.: Chronic carbon disulfide poisoning, J. Occup. Med. 14.123, 1972.
8. Calley, D., *et al.*: Toxicology of a series of phthalate esters, Chem. Abstr. 64:11749c, 1966.
9. Cook, W. A., *et al.*: Occupational acroosteolysis. II. An industrial hygiene study, Arch. Environ. Health 22:74, 1971.
10. Cornish, H. H., Dambrauskas, T., and Beatty, L. D.: Oral and inhalation toxicity of 2-*N*-dibutylaminoethanol, Am. Ind. Hyg. Assoc. J. 30:46, 1969.
11. Creech, J. L., Jr., and Johnson, M. N.: Angiosarcoma of liver in the manufacture of polyvinyl chloride, J. Occup. Med 16: 150, 1974.
12. Deece, D. E., and Joyner, R. E.: Vinyl acetate—a study of chronic human exposure, Am. Ind. Hyg. Assoc. J. 30:449, 1969.
13. Dinman, B. D., *et al.*: Occupational acroosteolysis. I. An epidemiological study, Arch. Environ. Health 22:61, 1971.
14. Dodson, V. N., *et al.*: Occupational acroosteolysis. III. A clinical study, Arch. Environ. Health 22:83, 1971.
15. Eckardt, R. E., and Hindin, R.: The health hazards of plastics, J. Occup. Med. 15: 808, 1973.
16. Fox, A. J., Lindars, D. C., and Owen, R.: A survey of occupational cancer in the rubber and cablemaking industries: Results of a five year analysis 1967–1971, Br. J. Ind. Med. 31:140, 1974.
17. Gerarde, H. W.: *Toxicology & Biochemistry of Aromatic Hydrocarbons* (New York: Elsevier Publishing Company, 1960).
18. Goto, S., Hotta, R., and Sugimoto, K.. An Aetiologic Factor Responsible for Retinal Microaneurysm due to Carbon Disulfide, Second International Symposium on Toxicology of Carbon Disulfide, Yugoslavia, Banja Koviljaca, May, 1971, pp. 25–28.
19. Hamilton, A.: Introduction to viscose rayon survey in Pennsylvania. Pennsylvania Department of Labor and Industry, Bulletin No. 46, 1938.
20. Harris, D. K , and Adam, W. G. F.: Acroosteolysis occurring among men engaged in the polymerization of vinyl chloride, Br. Med. J. 3:712, 1967.
21. Hernberg, S., Nurminen, M., and Tolonen, M.: Excess mortality from coronary heart disease in viscose rayon workers exposed to carbon disulfide, Work-Environ.-Health 10.93, 1973.

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