

REPORT OF VISIT
TO
CHINA GULF PLASTICS CORPORATION
April, 1974

R. L. Gibson, M.D.

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SUMMARY

In the U. S. the National Institute of Occupational Safety and Health (NIOSH) and the Occupational Safety and Health Administration (OSHA) have given top priority to vinyl chloride since January of this year when the B. F. Goodrich Chemical Company of Louisville, Kentucky reported that three employees who had worked in the manufacture of polyvinyl chloride resins for over twenty years had died of angiosarcoma of the liver. Subsequently industrywide investigations have disclosed several more cases of this rare liver cancer. NIOSH responded by rejecting a threshold limit for vinyl chloride and recommending that any employee exposed to measurable amounts of vinyl chloride should wear an air-supplied respirator. On April 5th OSHA issued an emergency health standard reducing the TLV for vinyl chloride from 500 ppm. to a 50 ppm. ceiling level and advised industry that enforcement would begin immediately. Several research studies, sponsored by industry, government and universities are currently underway to define the extent of the problem and safe exposure levels. Preliminary findings seem to indicate that these levels will in all likelihood approach zero.

Visits to CGPC manufacturing facilities in Taiwan reveal potential exposures to a variety of chemicals including vinyl chloride monomer and polymer, solvents, mercury and stabilizer compounds and actual exposures to these chemical agents and others were confirmed by the industrial hygiene survey. The need to establish medical and environmental surveillance procedures similar to those presently proposed in the U. S. is apparent and appropriate medical and industrial hygiene engineering recommendations are made. Engineering and work practice procedures to reduce these chemical exposures should receive top priority along with the medical examination programs which are necessary to furnish evidence of a successful environmental effort. At the same time CGPC will need to provide trained personnel and adequate medical facilities to carry out these tasks and proposals are set forth to accomplish these objectives.

RECOMMENDATIONS

Medical Considerations

1. The medical facilities at Toufen Factory should be expanded to provide at least two physicians' offices, examining rooms and a toilet.
2. A second full-time, English-speaking physician should be hired as soon as possible primarily to carry out the preventive medicine program. Preferentially he should be based in Toufen but cover all the plants by making periodic visits. At an early opportunity, once CGPC is satisfied with his performance, he should be sent to the U. S. for a minimum of one month's training under the auspices of the Gulf Medical Department.
3. As soon as the medical personnel and facilities are available CGPC should initiate programs of preemployment and periodic physical examinations to be conducted on-site at the Toufen Factory and extended when practical to other CGPC locations. These programs should begin as soon as possible this year.
4. The nurses at the Toufen Factory should be trained to perform urinalyses, initially using dip-stix (Ames) tests, and possibly later doing microscopic urinalysis.
5. All workers should have a standard preemployment physical examination including a medical history, physical examination, chest x-ray, serology and urinalysis. Consideration might be given to translating the Gulf Medical Examination Form (Gulf 56118B) into Chinese for this purpose.
6. All workers exposed to toxic chemicals including solvents, mercury, stabilizer dusts, VCM and PVC should have preplacement and annual physical examinations. The Gulf Medical Form can also be used for these exams and contains questions pertinent to the toxic symptoms and signs resulting from these chemical exposures. For example, these exams should include a medical history and physical examination with emphasis on the following items:

Solvents - headaches; nausea, dizziness; skin and mucous membrane irritation; urinary symptoms and signs relative to the cardiorespiratory, gastrointestinal and genitourinary systems.

Mercury - weight loss; insomnia; tremor; personality change; loss of appetite and urinary symptoms and signs.

Dusts - loss of appetite, metallic taste; constipation; insomnia; weakness; irritability; muscle and joint pain; abdominal pain; wrist drop; and symptoms and signs relative to the respiratory and genitourinary systems.

VCM, PVC - alcohol intake; hepatitis; previous chemical exposures; blood transfusions; symptoms and signs relative to the gastrointestinal systems with particular attention to the liver.

All workers receiving these annual examinations should also have a urinalysis, complete blood count, serology, and chest x-ray. In addition, the following groups should have studies done as follows:

Solvent Workers (100 estimated) - An annual SMA-12 profile blood test.

Stabilizer Dust Workers (30 estimated) - blood lead analyses done initially to assess exposures following engineering controls. The need for further testing will be based on the results of these initial tests.

VCM Workers (40 Toufen and 220 TVCM plants estimated) Annual SMA-12 profile, annual bilateral PA hand x-rays on all current and former reactor cleaners only.

PVC Workers - (44 Toufen and 80 Taoyuan estimated) An annual SMA-12 profile.

If the VCM or PVC workers have been exposed for 10 years or more in any company then the laboratory studies should be repeated every 6 months.

In general, if one or more tests are abnormal the studies should be repeated as soon as possible. If they remain abnormal the worker should be removed from the exposure and the cause of the abnormality investigated. If the repeat test is not abnormal, it should be rechecked in 6 months.

7. An attempt should be made to secure a copy of the death certificate as soon as practical following the deaths of all VCM and PVC employees and former employees whenever possible. Copies of these certificates translated into English should be reviewed by the CGPC medical advisor for suspicious causes of death. Further inquiry into these cases may be necessary.

8. A system of recording sickness and accident absenteeism should be established. Such records should indicate both frequency and severity rates for the total employee population as well as specific exposures of interest, e.g. VCM, PVC, solvent, dusts and mercury.
9. The new occupational safety and health act for Taiwan should be translated into English and reviewed by CGPC and the Gulf Medical Department as soon as possible.
10. An oxygen resuscitation and aspirator should be purchased for the Toufen Medical Department.
11. First-aid equipment should be placed in key locations in the plants and maintained by safety or medical personnel. All supervisory personnel should be given a formal first-aid course on-site.
12. Vehicles on-site should be equipped for stretcher cases and stretchers should be available.

Industrial Hygiene Considerations

1. Dr. Robert Cheng's recommendations to reduce exposures to solvents, mercury, stabilizer dusts, VCM and PVC should receive top priority and be implemented as soon as possible. It seems apparent that most, if not all, of the recommendations set forth in the NIOSH health standard for the manufacture of synthetic polymer from vinyl chloride will soon become U. S. regulation and CGPC should consider instituting these procedures in a practical, step-wise fashion.
2. An environmental surveillance program as recommended by Dr. Cheng should be initiated as soon as equipment is available but the sooner the better. Initially environmental measurements will have to be done frequently until the exposures are defined and within acceptable limits.
3. One or more employees should be assigned responsibility for the environmental surveillance program for all plant locations. In view of the scope of the CGPC operations, the inherent health risks, the international publicity on VCM toxicity and the absence of industrial hygiene backup in Taiwan, I recommend that one employee, preferably a chemist or engineer, who speaks and understands English, be sent to the U. S. for a minimum of 3 months for intensive industrial hygiene under the auspices of the Gulf Medical Department. This will improve the quality of the

program, establish lines of communication and put CGPC in an advantageous position when dealing with the DOL and/or NHA. Dr. Cheng should return to Taiwan later this year either during or following the engineering changes and reevaluate the in-plant environmental situation.

4. Records should be kept in writing both in Chinese and English of the results of all environmental monitoring and retained indefinitely.
5. Employees should be advised in writing of the risks of all toxic exposures and advised to report all related symptoms and signs immediately.
6. Each plant location should request from the Medical Department those Health and Safety Data Cards pertinent to its operations. At the same time a list of all chemicals purchased by each plant should be available in the plant for review.
7. Approved ear defenders, either muffs or plugs, should be available for workers exposed to noise exceeding 90 DBA.
8. Bacteriological examination of "potable" water sources at all plants should be done periodically, but not less than 4 times yearly depending on the findings.
9. Treatment facilities for all human and industrial waste should be given a high priority.
10. Access should be restricted by posting notices to all potentially hazardous areas, particularly those areas with VCM exposures.
11. Workers in potentially hazardous areas should not be permitted to eat on the job under any circumstances.
12. Hand-washing and shower facilities should be readily available to workers at each facility and plant location.
13. All workers should be issued lockers.
14. An educational effort should be made to promote personal hygiene measures in the plants.
15. Uniforms should be changed frequently and consideration given to a Company-sponsored laundering program to assure safe handling and to avoid contamination in the homes of the workers.

BACKGROUND

VINYL CHLORIDE

On January 24, 1974 the B. F. Goodrich Company announced that it was investigating the possibility that the cancer deaths of three workers at a plant in Louisville, Kentucky were related to their work with polyvinyl chloride. The diagnosis of a rare liver cancer, angiosarcoma, was confirmed by autopsy in all three cases. Previous to the public announcement which was widely reported in the press,¹ Goodrich medical representatives had informed Kentucky health officials and the National Institute of Occupational Safety and Health (NIOSH). Both organizations immediately responded by sending teams of experts to the plant. At the same time an effort was initiated to determine the extent of angiosarcoma in the U. S. and foreign countries with similar manufacturing processes. The Labor Department also responded by proposing an emergency fact-finding hearing to be held on February 15th to examine the extent of worker exposure to vinyl chloride and by sending industrial hygienists to the plant to determine if there was a violation of federal standards.

By mid-February the industry survey had disclosed 3 more cases of angiosarcoma and 50 abnormal liver tests in workers exposed to polyvinyl chloride at the Goodrich Plant in Kentucky. On February 19 the Kentucky Standards Board at an emergency meeting adopted a 50 ppm. time-weighted average (TWA) and a ceiling value of 75 ppm. for 15 minutes for vinyl chloride.² A value of 200 ppm. without use of protective equipment was set as an imminent danger situation. The value of 50 ppm. was based on animal toxicological studies by Doctors Viola and Maltoni. On February 22nd NIOSH held a meeting of all interested parties in Cleveland, Ohio to review the situation.

On March 1, the MCA sponsored a meeting on PVC decomposition products in Washington, D. C. Spokesmen for 12 firms acknowledged that a problem existed and expressed their interest in a PVC decomposition project. On March 11th NIOSH sent a standard³ for the manufacture of synthetic polymer from vinyl chloride to the Occupational Safety and Health Administration (OSHA) which principally recommended that any employee exposed to measurable amounts of vinyl chloride should be required to wear an air-supplied respirator. The concept of a threshold limit for vinyl chloride was rejected. NIOSH also announced it would conduct a study to evaluate the degree of protection afforded by different types of respirators using vinyl chloride as the test gas. On March 22nd NIOSH

issued a recommendation for medical surveillance⁴ of workers exposed to vinyl chloride.

On April 5th OSHA issued an emergency temporary health standard⁵ to become effective April 8th reducing the TLV for vinyl chloride from 500 ppm. to 50 ppm. ceiling at the same time proposing a permanent standard that would not allow workers without protective equipment to contact vinyl chloride in any measurable concentration. Both standards cover workers involved in the manufacturing of vinyl chloride and its conversion into polyvinyl chloride. By law the temporary standard can remain in effect up to 6 months while a permanent standard is being formulated; however, the DOL plans to expedite the procedure to a period of 2 to 3 months. Assistant Secretary of Labor, John Stender said "the emergency standard will serve to protect workers from the grave danger we know exists." Further Stender indicated that his field people would begin checking work practices in the entire vinyl industry almost immediately. Senator Henry Jackson said that the emergency standard "leaves too much to chance" and on April 9th told a United Rubber Workers group that legislative moves will be considered if workers continue to be used for "experiments" in the name of occupational safety and health. Further he stated that any standard dealing with vinyl chloride should "err on the side of safety." Both B. F. Goodrich and Goodyear announced they had reduced vinyl chloride levels to below the 50 ppm. before the publication of the emergency standard and that they were providing protective equipment and clothing to employees. Dow said it has used the 50 ppm. standard for 15 years in its U. S. plants.

A national surveillance registry⁶ for cases of angiosarcoma was also established by NIOSH and the U. S. Center for Disease Control (C.D.C.) in Atlanta. Physicians who have patients under their care with a diagnosis of angiosarcoma of the liver, or who have encountered such cases in their practice over the past 10 years, are urged to report them to CDC. As of early April, 1974 NIOSH reported 10 angiosarcomas attributed to vinyl chloride exposure. Of the total 7 cancers were discovered at the Goodrich plant in Kentucky, 1 at Union Carbide in South Charleston, West Virginia and 2 at a Goodyear plant in Niagara Falls, New York. In addition, 1 case has been discovered in Great Britain and several possible cases were reported in Germany. None of the reported cases in the U. S. were exposed less than 10 years in various phases of the vinyl chloride polymerization process.

The Society of the Plastics Industry (SPI) met repeatedly with the Food and Drug Administration (FDA) officials early in 1974 to review the VCM situation. Based on the

experimental evidence the FDA concluded on March, 1974 that VCM is a carcinogen. An interim food additive regulation was proposed and a suitable toxicological protocol was requested. The need for a literature survey had been previously discussed as well as toxicological studies to determine whether VCM is in fact a carcinogen for the rat when the route of exposure is via the diet. Toxicology protocols for 90 day feeding studies were submitted by Food and Drug Research Laboratories, Inc. to SPI on February 12th to satisfy the food additive regulation.

On April 16th an SPI Vinyl Chloride and Polyvinyl Chloride Producers Ad Hoc Committee met in Washington for the purpose of considering the industrywide problems associated with the emergency temporary standard set by OSHA. Working committees were set up to gather data regarding levels of exposure in VCM and PVC plants as well as VCM residual levels in various polymer products shipped by the polymerization plants. In addition, a working group is also investigating the nature of any VCM problem that might exist in the plants of vinyl processors; if any problem should be found to exist in such plants, an attempt will be made to isolate the sites within the plants that might require special attention. Still further, another working group is investigating the economic impact if the standard should be significantly lowered to a level where polymerization could no longer remain in production, or if permanent standards should be set at a "no detectable" or 1 ppm. monomer level in air, using methods sensitive to 1 ppm.

On April 22nd a meeting was held between SPI representatives and OSHA to explain SPI's intended participation. The SPI reported that OSHA is anxious to propose a permanent standard that strikes a fair balance between the need to protect workers in PVC plants without making it economically impossible for the industry to continue. OSHA advised that, in the absence of any data on which to fix a "safe working level" and in the light of the MCA-sponsored data casting doubt on the safety of the 50 ppm. emergency standard, OSHA will propose a 1 ppm. peak exposure limit combined with a 40 ppm.-hour limit per week. It is now anticipated that a proposal will be in the Federal Registry this May.

The Environmental Protection Agency (EPA) has also formed an internal task force to look into the effects of not only the health risks associated with the manufacturing of vinyl chloride but also possible environmental risks associated with the distribution and disposal of VCM and PVC. The task force plans to meet with environmental

and consumer groups and the chemical industry to discuss its mission and exchange information. It is also working with OSHA, NIOSH, the Consumer Product Safety Commission and the Department of Commerce. The EPA currently registers 23 pesticide aerosols using vinyl chloride as a propellant and on April 24th recalled all pesticides containing vinyl chloride. In addition, Dr. D. Wesley Clayton, EPA, Office of Research & Development, stated that he believed it was possible to establish a safe level for carcinogens. One EPA official noted that monitoring of water near vinyl chloride plants revealed between 2 and 3 ppm. vinyl chloride in water samples but evidently it survives in water for about 2 hours only.

METHYL BUTYL KETONE

In mid-August 1973, a worker in the printing department of the Columbus Coated Fabrics Plant, Borden Chemical Division, Inc., Ohio was seen on the neurosurgery service of the Ohio State University Hospital complaining of having been weak since May. Diagnostic studies confirmed acute peripheral neuropathy. Suspecting that a toxic agent might be responsible, Ohio State health officials performed electromyograms (EMG) on 1156 employees. Those with abnormal EMG's were given a neurologic examination. Tests revealed that 45 workers were severely afflicted and others to a lesser extent. Investigation showed that 35 of the 45 employees worked in the print department where a mixture of methyl ethyl ketone (MEK) and methyl butyl ketone (MBK) was used in large quantities as a solvent. MBK was first used in August 1972 and since no other changes in materials had occurred in recent years, MBK was implicated as the toxic agent.

The printing department was closed for one month in early September 1973 while MBK was removed from production materials and improved ventilation and work practices were instituted. Among the remedial measures are the wearing of respirators, rotation of workers required to wear respirators, company-provided protective clothing and provisions for eating meals away from work areas.

A total of 700 members of the 950 employees in the bargaining unit represented by the Textile Workers Union's Local 487 were off work, some for as long as two months and the Ohio State Industrial Commission ordered a hearing to determine whether the plant should be closed. Following a series of meetings in Washington, D.C. with federal mediators and representatives of OSHA and NIOSH, a union-management agreement was reached to abate the hazard and NIOSH was assigned to coordinate the new safety program. Since the

department's reopening in October 1973, no new cases of peripheral neuropathy have been discovered; however, on February 11th the union again went on strike ostensibly over safety and health issues, claiming that at least 10 workers were still seriously affected by peripheral neuropathy. Mediated negotiations in Washington, D.C. began again on February 25th. Borden Company representatives said that excessive union demands rather than health hazards at the plant might force its closing. The issue remains unresolved.

While NIOSH investigated the use of MBK in other areas of the country, Eastman Chemical Products, Inc. a manufacturer of MBK. instituted studies involving exposure of MBK, MEK and methyl isobutyl ketone (MIBK) of dogs, monkeys, rats and guinea pigs.⁷ Inhalation concentrations ranged from 1300 to 2000 ppm. for 6 hours a day, 5 days a week during a four-month period. Although results on the dogs and monkeys were inconclusive, all 6 rats showed changes characteristic of peripheral neuropathy. Exposures to MEK and MIBK did not produce conclusive results. Guinea pigs were treated with skin application of MBK during a 4 month period. Eastman Chemicals issued a letter on March 1, 1974 to its 2000 customers outlining the results of the study and recommending protective measures.

RETAIL MEAT WRAPPERS

In response to requests for health hazard evaluations of retail meat wrapping employees in and around Seattle, Washington, NIOSH conducted a limited study⁸ and concluded that the findings were generally applicable to all retail meat wrapping operations using PVC packaging films. It was determined that air contaminants generated by the thermal cutting of PVC packaging films in conjunction with the wrapping of meat are potentially toxic to some meat wrapping employees. The study primarily consisted of a literature review and examination of workers and work places. Evidence suggested that a sizeable percentage of meat wrappers suffer from upper and lower respiratory tract symptoms. An attempt was made to identify and quantitate air contaminants. Of the many additives, HCl and a plasticizer, di-2-ethyl hexyl adipate, were the predominant contaminants. Recommendations were made regarding lower cutting temperatures, improved ventilation and medical surveillance. Other similar studies around the country have been conducted and further investigation of affected workers is proposed.

ACROOSTEOLYSIS

Occupational Acroosteolysis^{9,10} is confined solely to workers engaged in the production of PVC from VCM and is characterized by bony defects of the extremities and Raynaud's phenomenon. The disease was first noted in 1963. In 1971 Dinman et al reported 25 definitive cases with an additional 16 "possibles" after an extensive survey sponsored by the MCA of 5011 workers in 32 U. S. plants. With one exception all workers with the disease were production employees who either were or had been reactor cleaners, an incidence in this group of 3 percent. The period of exposure to vinyl chloride polymerization before the onset of symptoms was variable, as short as one month or as long as 3 years. The disease is diagnosed by the characteristic x-ray findings, generally limited to the hands, forearms and sacroiliac joints. There is no specific treatment except removal from exposure which usually slows or stops its progression. Improvement in the bony defects can occur and some workers have been returned to reactor cleaning. Prevention consists of reducing exposures by protective clothing, discontinuing the use of chip hammers, and engineering controls, including solvent and steam cleaning which obviate the necessity of workers entering the reactors.

MINAMATA'S DISEASE

Between 1953 and 1960 methyl mercury in the effluent of a vinyl chloride plant poisoned 121 persons and killed 43 persons in Minamata, Japan. In addition, congenital defects were found in 23 babies whose mothers were exposed during pregnancy. The methyl mercury primarily accumulated in shellfish which were eaten by the local populace, birds and fish. No new cases of this disease have been reported since 1961.

In 1971 Yogamuchi¹¹ et al describes the recovery of methyl mercury compound from the sludge pit of a caustic soda factory in which only metallic mercury had been used in the electrolysis of sodium chloride. In this industrial situation the reaction occurred mainly in a sedimentation pit where a precipitate of calcium carbide is added to neutralize water from the electrolysis plant. Additionally trace amounts of methyl mercury have been produced experimentally in the reaction of inorganic mercury with amorphous carbon, the material of which electrodes in the electrolysis plant are fabricated. The EPA has published a national emission standard that limits atmospheric emissions of mercury to less than 2300 grams during a 24-hour period.

McGill et al found no evidence of dangerous absorption of mercury in workers in one chlor-alkali plant study. Air levels over a period of 6 years varied between 0.08 and 0.13 mg./m³ of Hg. as measured by a mercury vapor meter. Smith et al in a study of 21 chlor-alkali plants in the U. S. & Canada reported a positive correlation between exposure levels ranging from less than 0.01 mg./m³ of Hg. to 0.27 mg./m³ of Hg. and neurological involvement (tremor, shyness, nervousness), loss of weight and loss of appetite. The demonstration by Smith of toxicity at levels below 0.1 mg./m³ of Hg. and the occurrence of toxicity between 0.005 and 0.06 mg./m³ of Hg. reported by others resulted in the proposed NIOSH environmental standard of 0.05 mg./m³ of Hg. for protecting the health of exposed workers. The maximum allowable concentration for metallic mercury in the USSR which was established 30 years ago is 0.01 mg./m³.



VINYL CHLORIDE RESEARCH

A paper by Professor P. C. Viola¹² (March 1970 Medicina del Lavaro, Vol. 61, No. 3, pp. 174-179) confirmed the toxic effect of vinyl chloride in producing degeneration of bone and connective tissue with histopathological changes similar to those observed in human acroosteolysis. Of the twenty-five rats which were subjected to very high concentrations of vinyl chloride at 30,000 ppm. for one year, six showed skeletal changes. Thirteen rats died from cardiorespiratory complications and 2 from hemoperitoneum. On the basis of this study he recommended that manufacturing plants polymerizing vinyl chloride should reduce the TLV and encourage automatic cleaning of autoclaves.

In May, 1970 Professor Viola presented a paper¹³ at the International Cancer Congress in Houston which described a carcinogenic effect of vinyl chloride. The experimental conditions which produced the following changes were identical to those described in the first paper but in this paper he states that 65% of the animals developed tumors of the skin, mostly epidermoid carcinoma, and 26% of these showed tumors of the respiratory tract exclusively localized in the lungs and morphologically appearing as an adenocarcinoma. Very few animals developed bone tumors, localized in the metaphyseal region. No liver cancers were described.

In September 1970 an MCA Committee discussed Professor Viola's findings and determined that further research with lower concentrations of vinyl chloride should be done. Currently this program is being done by Industrial Bio-test Laboratories in Chicago and is financially supported in the amount of \$180,000 by contributions from 20 manufacturers of VCM and/or PVC. New participants, including Gulf are now being added to the program to help sponsor additional studies totalling \$80,000. Initial contributions are \$24.38 per million pounds of annual VCM plus PVC production capabilities. It is anticipated that an additional \$500,000 may be involved over the next 3 years. In a preliminary report announced by Bio-Test on April 16th, mice exposed for seven months, seven hours a day, five days a week, to 2500 ppm., 200 ppm., and 50 ppm. were showing liver angiosarcomas at all levels while none were reported in the exposed rats and hamsters.

Another MCA proposal to study the metabolic processes by which vinyl chloride reacts with biological systems has been prepared by the Dow Chemical Company and endorsed by the Technical Task Group of the MCA. In a related proposal Dow has also offered to conduct a small teratology

study. These requests will entail a commitment of \$80,000 from the supporting companies (metabolic studies \$50,000, teratology studies \$20,000, contingency studies \$10,000.)

Tabershaw-Cooper Associates were also contracted by the MCA to conduct a mortality study of workers engaged in VCM and PVC manufacture at an estimated cost of \$93,340. The objectives are (1) to compare the mortality of individuals who have worked in vinyl chloride plants with the general population (2) to compare mortality patterns within the population of vinyl chloride workers based upon exposure, and (3) to compare the mortality of VC workers with other occupation groups. The final report has been delayed since the study is now being revised as previously described to review all suspicious cases of malignancy. A preliminary review of the data indicates that the overall mortality figures will be comparable to those of the general population.

NIOSH is engaged in several vinyl chloride research efforts. Dr. Edward Fairchild is initiating a review of the available literature regarding the toxicological effects of PVC. NIOSH is undertaking a study of plants that have had PVC operations for 15 years or more and will review records of former workers in PVC plants. It is also evaluating respiratory protective equipment. As mentioned before NIOSH through CDC has also started a national surveillance registry for cases of angiosarcoma of the liver.

A medical research program on angiosarcoma and related liver abnormalities is also being organized by the University of Louisville's Health Sciences Center and Cancer Center under a grant from the B. F. Goodrich Company. The first year of the program will cost an estimated \$300,000. Eventually broader support may be sought.

At the OSHA public hearing in Washington on February 15th Professor Cesare Maltoni, Istituto Di Oncologi, Bologna, Italy, reported on a series of experiments on the effect of exposure of rats, mice and hamsters to VCM at concentrations of 10,000; 6,000; 2,500; 500; 250; and 50 ppm. for varying periods of time. The results so far indicate that tumors have been observed in groups of animals exposed to VC at concentrations as low as 250 ppm. No tumors have been observed at 50 ppm. He is now repeating this work with 300 animals at 50 ppm.

Other organizations in the U. S. involved in vinyl chloride research include the University of North Carolina under the sponsorship of the Rubber Workers Union and the American Cancer Society.

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UNION ATTITUDES IN THE U. S.

When the announcement of the Goodrich cases was made, Louis Beliczky of the United Rubber Workers union said, "I look at this as the dropping of a bomb. It opens up the possibility of a whole new occupational disease." Further he suspected a connection between the Goodrich and Borden problems.

Dr. Irving Selekoff, Mt. Sinai School of Medicine, New York, N.Y., said there has been evidence of potentially serious disease among workers engaged in vinyl chloride manufacture for 25 years which has been incompletely appreciated and inadequately approached by medical scientists and regulatory authorities. Acute animal toxicity to vinyl chloride was reported as long ago as 1938 and important chronic toxicity was reported in 1961, Selekoff said. As far back as 1949 liver damage was found in 15 of 48 exposed workers in Russia and disease of the liver, skin and other organs was reported in the next 17 years from Rumania, Russia and France. Recent studies in Germany have shown that liver damage is far more common and far more serious than was expected. He recommends no further exposure by any route and emphasizes that no control should be considered too rigorous.

Sheldon Samuels, Director, Health, Safety and Environmental Affairs of the AFL-CIO's Industrial Union Department (IUD), submitted a petition to OSHA on behalf of IUD and the United Rubber Workers for an emergency standard for vinyl chloride. Anthony Mazzocchi of OCAW also called for an emergency standard. "What we now know about the relation between cancer and vinyl chloride is only the tip of the iceberg because of the long latency period," Mazzocchi said.

On publication of the temporary emergency standard Sheldon Samuels charged that the measure was ineffective and that the DOL had misinterpreted the Italian research; however, he did praise the proposed tougher permanent standard as "an important step forward." The committee on carcinogens of the IUD appealed to Congress for an immediate emergency appropriations bill to deal with the recently discovered hazards of vinyl chloride and related carcinogens. Peter Bommarito, President of the United Rubber Workers said, "we feel that very soon current animal studies will verify the real risk to humans at the 50 ppm. level" and urged that the standard be immediately expanded to include the NIOSH work procedures and medical surveillance recommendations. At a meeting on April 2nd in Mt. Sinai Hospital 12 union representatives agreed to fight the proposed 50 ppm. temporary standard. Stephen Wodka of OCAW announced

that "OCAW would not support any position that allows any such standards to go forward. The Committee said legal action might be taken if the 50 ppm. standard was promulgated. In addition the group called for medical surveillance of all American workers exposed to vinyl chloride to begin immediately. Dr. Selekoff said that preliminary data indicates that 5 percent of all deaths of vinyl chloride workers may result from liver cancer and that other operable disorders apparently result from exposure to the substance. Beliczky said that the unions should have access to whatever exposure data corporations have but doubted if the information is valid and accused the employers of faulty sampling methods.

U. S. CONTACTS

The following medical authorities on vinyl chloride were contacted for information on the current situation:

1) Dr. Marcus Key, Director of NIOSH - NIOSH's recommendations for medical surveillance were reviewed and are included in this report. The research on respiratory protective devices will begin soon but the date of completion is uncertain. Dr. Edward's Committee on Toxicology now believes (April 1974) that there may be an acceptable level for carcinogens other than zero, but one which will likely be close to zero. Although there is no agreement as yet on the number of experimental animals necessary for statistical purposes, if Maltoni had conducted his studies on 500 to 800 animals instead of 64 and had no effect at 50 ppm. and a 1/50 safety factor allowed, then NIOSH might recommend a ppm. level for VCM (1/50 is a compromise between the FDA safety factor of 1/100 for natural carcinogens and the ACGIH safety factor of 1/10 for non-carcinogens). Undoubtedly this attitude will change with consideration of the recent Bio-Test findings of tumors at 50 ppm.

2) Dr. Clark Cooper of Tabershaw and Cooper, Inc., a private consulting firm. This firm had been conducting an MCA-sponsored mortality study of the vinyl chloride industry prior to the cancer incident. They are now reviewing the death certificate data for suspicious causes of death, e.g. carcinomatosis, hepatomas, liver deaths without autopsies, etc. They are also studying the death certificates of all workers who previously were diagnosed as having acroosteolysis.

Dr. Cooper was gloomy about liver function tests for early detection of liver cancer but believes they must be done to establish baseline values and to demonstrate an awareness and interest in the problem. He would continue, however, to rely more on the medical history, asking questions regarding weight, appetite, fatigue, etc. He emphasized that the major emphasis must be to reduce exposures.

3) Dr. Maurice Johnson, Medical Director, B. F. Goodrich Company - Medical surveillance procedures were reviewed. All workers exposed to VCM or PVC are receiving an annual medical evaluation consisting of a medical history, physical examination, chest x-ray, urinalysis, CBC and SMA-12 profile. Liver function tests include a serum bilirubin, SGOT, SGPT, Alkaline phosphatase and a new test, GGTP (gamma glutamyl transpeptidase). Dr. Johnson emphasized that laboratory tests are rarely

abnormal in angiosarcoma cases and that it is necessary to quiz for symptoms; however, one of the Goodrich cases had a slight elevation of LDH which led to a positive biopsy. Two of the Goodrich cases are living and blood serum studies for antigen activity are being conducted by the National Cancer Institute.

All Goodrich workers exposed to VCM now receive a single PA hand x-ray annually. The frequency was initially every 6 months and may be extended to a biennial program since no cases have been found for 2 years. A medical history and physical examination have not been done in the past on this group but will be done in the future as discussed above. Some of the original cases of acroosteolysis which have shown considerable x-ray recovery have been returned to VCM work.

- 4) Dr. Carl Dernehl, Associate Medical Director, Union Carbide - (Contacted by Dr. W. McClellan) - He reported one angiosarcoma in a Union Carbide Employee and 9 total U. S. cases and 1 U.K. case as of March 20, 1974. All cases were in workers around the polymerization process who were exposed between 10 and 22 years. He believes there is a threshold dose between 10 and 50 ppm. There were no consistent symptoms or signs and only one of the cases had a history of hepatitis. Pathological study confirmed angiosarcoma and revealed a diffuse liver fibrosis. Union Carbide was advised by the FDA that vinyl chloride will be considered a carcinogen and proposed a limit of 50 ppb in foodwrap.
- 5) Dr. Thomas Milby, the Hine Laboratories, Inc., San Francisco, California - He confirmed that their laboratory would be able to ship containers to Taiwan for the collection of blood and urine samples to be analyzed in California for lead and mercury, respectively. The cost for these analyses will be \$10 each for blood and/or urine leads and \$12 each for urine mercury. A discount of 20% will be given if the number of samples in any category exceeds 10. They would also bill for shipping charges to Taiwan.
- 6) Dr. Ralph Erickson, Chief of Pathology, Western Pennsylvania Hospital - We discussed the new gamma glutamyl transpeptidase (GGT) test of liver function. This test is nearly specific for liver and biliary tract disease causing intrahepatic obstruction and is particularly accurate for acute alcoholic hepatitis. Elevations, however, are sometimes seen following myocardial infarction. The hospital first offered this test in March 1974 at a cost of \$8.00.

TAIWAN CONTACTS

- 1) Dr. C. H. Yen, Director General, National Health Administration (NHA) - A meeting with Dr. Yen was arranged to advise him of our Company's concern with respect to occupational health in general and to the vinyl chloride problem in particular. He was fully aware of the current situation in the U. S., having recently visited with Dr. Marcus Key at NIOSH in Washington and reviewed vinyl chloride literature. Additionally both the Chinese and English edition newspapers in Taiwan have had front page articles describing the problem. He was pleased that the CGPC was actively engaged in an early preventive effort and offered his help should it become necessary.

He is vitally concerned about the lack of occupational health services on the island and discussed a proposal now under consideration to seek government, university and private support for an independent occupational health consulting service to be established in the National Taiwan University. This program would ultimately provide occupational medicine and industrial hygiene consultation and a full range of laboratory services for both government and industry. A major roadblock to date has been the reluctance of the Ministry of the Interior to co-sign an agreement with the NHA since they evidently wish to remain independent; however, they are expected to sign within two months. Philco is presently sponsoring the training of two industrial hygienists at the University of Washington in Seattle, both of whom will hopefully return to Taipei and initiate the program. At that point, or perhaps sooner, the Company can anticipate being asked along with other industry for on the island financial support for this effort.

Dr. Yen is a Graduate of Peking National University and has devoted his professional life on the mainland and in Taiwan to public health. He served as Commissioner of Health for Taipei for many years prior to his present appointment. He also held assignments for WHO in Geneva and Manila.

- 2) Dr. Cheh-Teh Loo, Director, Taiwan Veterans General Hospital - I met General Loo at his office in the Kohlberg Medical Research Laboratory which is adjacent to the Veterans General Hospital. The major purpose of the visit was to determine if the hospital could perform laboratory tests for CGPC. I was told by General Loo that this could be arranged and costs were generally discussed.

While the mission of the Veteran's General Hospital is to render diagnosis and definitive treatment to patients under the care of the Vocational Assistance Commission for Retired Servicemen (VACRS), private patients are accepted for both inpatient and outpatient care. This 996 bed hospital is located in suburb of Taipei called Shipai. It is a modern facility with a staff made up of 220 doctors, 353 nurses, 153 nursing attendants and 181 technologists. The average cost per day for veteran patients is \$NT 170 (\$U.S. 4.49). All professional medical and surgical services are provided by the hospital. Clinical laboratory services are extensive considering that special investigation can be referred to the Kohlberg Research Laboratory. An SMA-12-60 auto-analyzer is in use in the hospital.

A Laboratory Department Price List gives the following price quotations for several of the tests of interest to us:

a. Complete blood count (CBC)	\$NT 33 (\$U.S. 0.87)
b. Erythrocyte Sedimentation Rate	\$NT 15 (\$U.S. 0.40)
c. Serum bilirubin	\$NT 15 (\$U.S. 0.40)
d. SGOT	\$NT 30 (\$U.S. 0.80)
e. SGPT	\$NT 30 (\$U.S. 0.80)
f. Alkaline phosphatase	\$NT 30 (\$U.S. 0.80)

General Loo indicated that an SMA-12 profile would cost approximately \$U.S. 12.00. He offered to send technicians to the plant at minimal additional expense to obtain the blood samples from the workers. He felt that this would assure that the specimens were collected, labeled and eventually reported correctly. He further advised that the hospital did not do GGTP, lead or mercury analyses and suggested contacting the Navy Medical Research Unit (NAMRU-2) for advice on this.

- 3) Captain Raymond Watten, Commanding Officer, U. S. Navy Medical Research Unit (NAMRU-2) - Dr. Watten reviewed the mission of NAMRU and informed me that personnel were being immediately reduced from 250 to 200 because of a critical lack of research funds. Since he is retiring in two months he suggested I talk to other responsible persons in NAMRU to determine if they could offer laboratory support. He indicated a degree of optimism by saying that NAMRU might be able to analyse blood samples for the Company providing we either furnished or purchased the reagents. A tour of the laboratory which followed revealed an adequate capability for out laboratory needs. Further discussions with NAMRU personnel (Commander Berg, Chief of Pathology and Captain Blackwell, Hematologist)

and Dr. Palmer Beasley, Associate Professor, University of Washington, revealed that they would not be able to do the work because of the personnel cutback unless the Company was willing to hire a full-time technician, based in NAMRU for this purpose. They were advised that we would continue to seek other alternatives.

Dr. Beasley is Board Certified in Internal Medicine and Preventive Medicine and is engaged in hepatitis research in Taiwan. He is also vitally interested in establishing an occupational health capability on the island. The results of his research are of significance to our industrial medical surveillance program. Hepatitis B antigen has been found in 15 to 20 percent of persons of working age. Of these 10% have abnormal liver function tests, or about 2 percent of the total. This compares with the Philco experience of 3 percent positive liver function tests in their employees working with solvents. Since autopsies are not commonly done the incidence of primary hepatoma is unknown; however, it is either the first or second most common malignancy - nasopharyngeal cancer is the other - and one person stated that it comprised 20% of all reported malignancies in adult Chinese population.

4. Dr. Herbert Northrup, Medical Director, Philco - Dr. Northrup has made several visits to Taiwan following an incident in 1972 in the Philco television plant near Taipei in which 5 women working with solvents died of acute liver disease and 19 women were ill. Following the incident 200 employees quit work and absenteeism ran about 500/day. The plant was subsequently shut-down for several days. While it was never definitely established that the solvent was responsible for the deaths -- no autopsies were done-- and Philco strongly feels otherwise, the experience has cost Philco \$2 million to date. There are now 2500 employees at the Philco plant. Philco does all of the preemployment and periodic (annual) physical examinations at the plant. Laboratory studies including liver function are done at the suburban branch of the McKay Hospital which is adjacent to the plant. In addition an improved reporting system was established for all cases of suspicious illness.

In the past, Dr. Northrup arranged for blood specimens for workers in the Ford plant on the island to be sent to Dearborn, Michigan for blood analysis after poor experiences in the U. S. Navy Hospital in Taipei and in Japan. Recently the DOL has ordered Ford to renew this blood lead testing program.

5. Dr. Chen-Hui Lui, Professor, Department of Medicine, National Taiwan University - Dr. Lui is a hematologist and is currently Director of the Clinical Laboratory of the College of Medicine. I toured this laboratory to determine its acceptability for conducting our biological tests. While Dr. Lui affirms their ability to perform nearly all laboratory procedures, including heavy metal analyses, it is not up to the standard of the Veterans General Hospital in terms of technical personnel or equipment. There is no SMA-12-60 although one apparently has been on order for some time. A room with a spectrophotometer for testing heavy metals is cluttered with motorized equipment which undoubtedly would contaminate the samples. In my opinion the use of this laboratory at this time would be a poor alternative.

Cost estimates were given later by Dr. Chen over the telephone: CBC (rbc, wbc, Hb., Ht.) \$NT 100 (\$U.S. 2.64); liver profile \$NT 450 (\$U.S. 11.87); blood lead \$NT 200 (\$U.S. 5.28); urine mercury \$NT 200 (\$U.S. 5.28).

6. Dr. George Hahn, Country Hospital, Taipei - Dr. Hahn is an internist, cardiologist, and former Director of the Country Hospital and is well known to many of the Gulf families living in Taipei. Recently he has been conducting management health and overseas medical examinations and appears to be doing a very thorough workup. I toured the hospital and in particular reviewed the laboratory as a possible alternative for our use. The laboratory is small and under the direction of a technician trained at the National University of Taiwan. Since there is no pathologist in charge, the technician is under the general supervision of the medical staff. Most standard hospital laboratory tests can be done and those which cannot have in the past been sent to the National Taiwan University or to NAMRU. Laboratory tests are extremely cheap, a routine blood count costs \$NT 50 (\$U.S. 1.32) and a liver profile (bilirubin, SGOT, SGPT, alkaline phosphatase, CF, TT, TP) \$NT 150-200 (\$U.S. 3.96 - 5.28). I am concerned that the cost, as in Toufen, may reflect the quality of the work. Dr. Hahn feels the laboratory is reliable but occasionally sends specimens outside for recheck.

OCCUPATIONAL HEALTH AGENCIES AND REGULATIONS IN TAIWAN

The National Health Administration (NHA) is charged with responsibilities similar to the U. S. Public Health Service and in the occupational health field it relates to NIOSH, although their capabilities are severely limited by the lack of trained or experienced people. The NHA has Divisions of Public Health and Occupational Health both on national and provincial levels. They do respond to health problems in industry but seldom conduct regular inspections.

The Ministry of Interior, Department of Labor (DOL) has responsibilities for occupational health corresponding to those of OSHA under the U. S. Department of Labor. The major functions are to promote occupational health and safety in Taiwan and to conduct inspections and enforce regulations. Inspections are principally conducted by the Provincial Industrial and Mining Inspectional Committee (PIMIC); the Taipei Municipal Inspectional Office which is concerned with public safety as well; and the Kaohsiung Industrial Export Processing Zone which has its own Industrial Health Clinic to take care of general health and preventive medicine in this area.

The China Industrial Safety & Health Association is a private organization funded by industry, primarily to offer training programs for safety supervisors, environmental pollution and boiler inspectors. It published a quarterly safety and health journal. The China Productivity Center is another private organization which provides training in industrial safety.

The School of Public Health in the National University of Taiwan offers about 6 hours of occupational health instruction to medical students. There is also a two year graduate course leading to a Masters Degree in Public Health which has courses in occupational health including field trips. This school is being promoted as the future training and service center for occupational health and industrial hygiene activities on the island.

Fundamental labor policies of the Republic of China can be traced to the Constitution of the Republic and include non-discriminatory freedom of employment; the right to work; freedom of association; a social insurance system; protection of women and children; and health protection. "The State, in order to improve national health, shall establish extensive services for sanitation and health

protection, and a system of public medical services." The policy of promoting industrial hygiene and occupational health is consistent with the provisions of this Article.

The following laws and regulations are concerned with occupational health and safety: Factory Law; Statute for the Enforcement of the Factory Law; Factory Inspection Law; Miner Field Law; Statute on Employee Welfare Funds; Statute on Labor Insurance; Regulation Governing Safety and Health Facilities in Factories; Provisional Standards Concerning Medical Facilities in Factories and Mines; Regulations governing hours of work for Boiler workers; Regulations on the Formation of Safety and Health Committees in Factories and Mines; Regulations on the Safety Control of Fireworks Factories; Regulations Governing Safety of Mines in the Taiwan District; Provincial Regulations on Base Wages; and the newly established Occupational Health and Safety Law. (April 1974). None of the above laws and regulations was available in English; however, they do establish standards similar to the U. S. OSHA regulations and in some cases are more restricting. The head of the company/factory is responsible for occupational health and safety and is subject to penalties, including prison sentence, for non-compliance. English translation of the new Taiwan OSHA will be necessary to evaluate the CGPC compliance situation.

CHINA GULF PLASTICS CORPORATION

China Plastics Corporation began operations in Toufen in 1966 for the purpose of producing PVC resin and fabricated products. In 1968 Gulf became part owner of the Company and the name was changed to China Gulf Plastics Corporation (CGPC). The Company has diversified and expanded operations and now produces over 25,000 metric tons of resin and fabricated products a year.

There are presently three CGPC office locations and five manufacturing plants in Taiwan in which GCPC has a financial and operating interest. The main office in Taipei employs approximately 150 persons. Branch sales offices are located in Taichung and Kaohsiung, principal cities in Taiwan, and employ an additional 50 persons. Manufacturing facilities are as follows:

TOUFEN FACTORY

This is the original China Plastics Corporation factory and is located on the northern part of the island, approximately 1-1/2 hours by train 100 kilometers southwest of Taipei, and 70 kilometers from Taichung. Mr. Wilbur Shyeh is the General Factory Manager. The plant produces vinyl chloride monomer (VCM) from local sources of calcium carbide and salt as well as PVC resin, fabricated and related products, including sheet, film, leather, sponge leather, pipe and fittings, floor tile, flake and liquid caustic soda, hydrochloric acid, liquid chlorine and special products.

There are currently 1200 factory employees, including 71 women, working 3 shifts of 8 hours daily, six days a week. Prior to April 1, 1974 all manufacturing employees worked 7 days, 8 hours daily, a week. The average age of the male factory workers was estimated to be 29 years and the average salary \$NT 3600/month (\$U.S. 95) per month. Turnover has been as high as 51% per annum but was 31% in 1973 and many workers quit after 2 to 3 years. There is a 40 day probationary period for new factory workers. The Company maintains dormitories on-site for about 250 staff and workers. Other benefits include a retirement plan (translated into English) with mandatory retirement at age 65 and voluntary retirement at age 60 or after 25 years of service (70 point system), a pension plan, two uniforms per year, holidays (17 days/year), medical services and inexpensive haircuts. Employees contribute 1/3, \$NT 50/month

(\$U.S. 1.32) and the Company 2/3, \$NT 100/month (\$U.S. 2.54) to a Labor Insurance Scheme which provides benefits in the event of child-birth, injury, disability, death and old age. Since 1956 inpatient hospitalization has been available free of charge to insured workers and free outpatient treatment in hospitals for employees, not families, was introduced in 1970. The Company also provides medical care for those families of employees who live on or near the factory, approximately 300 dependents. After one year of employment all workers are eligible for 7 days of personal leave and 40 days of sick leave per year with full pay. If an employee is ill more than 40 days the plant manager may grant 1/2 pay, but when the illness exceeds 6 months the worker is subject to discharge. Staff benefits include 5 days personal leave and 2 weeks sick leave per year. All work injuries and illnesses for both groups are fully compensated. A Welfare Committee meets periodically with representatives of the worker's union.

The factory is presently operating at about 50 percent capacity because of a lack of orders and consequently many workers were not doing their usual work but performing busy-work, e.g., trimming, maintenance, etc.

Medical personnel include one full-time physician (Dr. L. F. Tang), one part-time physician and two full-time nurses (Miss K. H. Chiu and Miss G. M. Fu). Dr. Tang completed medical school on mainland China and practices general medicine. Both nurses are Taiwan-trained. Dr. Tang's salary is slightly more than \$NT 10,000/month (\$U.S. 264) per month, the part-time doctor receives \$NT 4,000/month (\$U.S. 106) per month and the nurses make about \$NT 3,000/month (\$U.S. 79) per month.

The medical facility consists of 3 rooms -- an office and pharmacy combined and two treatment rooms. There are no physicians' offices, examining rooms or toilet facilities. Equipment is sparse and includes a single size E oxygen inhalator on a stand, a few medical instruments for wound treatment and suturing and a minimum of diagnostic equipment. Many drugs are available including cold medicines, antihistamines, cough syrups, antibiotics, intravenous fluids, ointments, etc. Narcotics and disposable syringes are not available. Sterilization equipment is old and cumbersome to use. Clinic hours are from 7:30 A.M. to 7:00 P.M. There is no ambulance on-site and the available minibus has not been adapted to handle stretcher cases.

Medical personnel are primarily engaged in the treatment of dependents, seeing about 30 to 35 patients daily. Employees are also seen for minor injuries and illness and

referred to local medical facilities approved by the Department of Labor for more serious problems. About 2 or 3 emergency cases a month are sent to the hospital by car or taxi. There are 5 medical and surgical hospitals within 15 to 30 minutes from the factory which are used for referral depending on the type of illness or injury. First-aid training of staff or workers is limited and given along with safety training. There are minimal first aid supplies around the plant. Laboratory studies are done in an outpatient laboratory in town which was visited and is completely inadequate and unreliable. An x-ray facility at a local surgical hospital utilizes modern Japanese equipment and is acceptable for ordinary x-ray procedures.

Medical programs include BCG for dependent children (between 5 and 10 new cases of tuberculosis are seen annually in the workers), preemployment examinations (height, weight, blood pressure, vision, heart and lung check, serology and chest x-ray) at a Labor Insurance Bureau approved facility; annual periodic exams (height, weight, blood pressure and chest x-rays for employees over 40 and biennial for employees under 40) also carried out at government approved facilities; and the recently instituted special exams of workers exposed to VCM (hand x-rays and liver tests) solvents, mercury and stabilizer dusts (urinalyses and blood counts every three months with liver function tests if positive). The cost of a blood count (rbc, wbc, hemoglobin, reticulocytes) and urinalysis (protein, bilirubin, urobilinogen, coproporphyrin) is \$NT 80 per person (\$U.S. 2.11). PA and oblique hand x-rays cost \$NT 40 (\$U.S. 6.33). The number of participants currently receiving special exams of this type are as follows:

Reactor workers	8
Solvent workers	69
Mercury workers	26
Stabilizer workers	51

Results to date indicate about 25% abnormal urinalyses, primarily positive for urobilinogen and coproporphyrin, fairly equally distributed between the groups; however, in my opinion these results are invalid because of the unreliable laboratory facility. This is also true for the 8 reactor workers who received liver function tests on April 2nd (bilirubin, SGOT, SGPT, alkaline phosphatase, cephalin flocculation, and Takatas. All 8 workers had a positive cephalin flocculation test and 7 of the 8 had a positive Takatas test. All other tests for liver functions were normal. These studies also are meaningless in view of the laboratory involved. All hand x-rays on the 8 reactor workers reviewed in the U. S. were normal. No biological lead or mercury analyses have been done to date.

Absenteeism at the Toufen factory is alleged not to be a significant problem. The majority of absences are evidently for military service -- one day every 3 months and/or 1 month periodically -- and there are more absences during rice harvest time in the North in July and October. Since records of sickness absences were not available the following review of sick leaves of workers in hazardous areas for 1973 was requested:

Record of Sick Leaves Requested by Workers
Working in Hazardous Areas - 1973

		<u>No. of Workers</u>	<u>Total Sick Leave in 1973</u>	<u>%</u>
1. Mercury	Chlor-Alkali 1) Electrolyser 2) HCl & Chlorine	41	6	14.6
2. Polymer	Polymerization 1) Raw material 2) Cleaning 3) Discharging PVC	16	6	37.5
3. Dust	Extrusion, Film, Leather, Formu- lation Master- batch	23	1	4.3
4. Solvent	Leather - Coating & surface treatment Film/Sheeting - Printing	96	30	31.3
5. Dopfume	Film/Sheeting - Mixer, Bambuary Mixing Roll, Calender	82	11	13.4
TOTALS		258	54	20.9

TOTAL NUMBER OF WORKERS IN TOUFEN PLANT - 1060

TOTAL SICK LEAVE OF WORKERS IN HAZARDOUS AREA % = 5.1%
TOTAL NUMBER IN TOUFEN PLANT

While the data seem to indicate a potential problem in the polymer and solvent working areas the number of polymer workers may be too few to be significant. Solvent workers, however, are known frequently to complain of headaches and these

figures may reflect valid sickness absences. Obviously, a uniform system of absence records due to illness needs to be instituted to substantiate these statistics.

Since 1970 employees have been advised orally of symptoms associated with solvent, lead and mercury exposures and asked to report any suspicious illness. The statement was made that the Company does not want to hide these potential problems from its employees.

No workers have died while actively employed since the factory began operations in 1966 and less than 10 have retired. While death certificates in the country do list a cause of death and are signed by a physician, autopsies are very uncommon. Additionally, annuitants are paid through an outside trust fund and consequently the trust fund, not the Company, would normally receive a copy of the death certificate. The Company would receive copies of death certificates of employees who die while actively employed but would have no way of obtaining death certificates on employees who die after leaving the company for reasons other than retirement.

A review of plant operations at the Toufen Factory confirms the engineering findings that there are considerable exposures to solvents, stabilizer dusts, mercury, DOP fume, VCM and PVC resin. There are also potential exposures to a large variety of chemicals including printing inks, chromic acid and hydrogen cyanide. In addition, present work practices may enhance the exposures. Long hours (formerly 56/week and now 48/week), lack of convenient sanitary facilities (lockers, washbasins, showers), eating on the job and no uniform change or laundering policy all contribute to the possibility of overexposures.

The industrial hygiene engineering survey conducted by Dr. Robert Cheng confirms my observations that the following areas or operation are of greatest concern:

1. Leather room - three calenders and a forming oven; exposures to solvents, primarily MEK, DOP, inks, PVC, stabilizer dusts. Ventilation around the troughs is inadequate; men eat on the job; washing facilities not immediately available; housekeeping good.
2. Film room - three calenders; exposures to DOP, PVC and stabilizer dusts; ventilation over calenders probably adequate; housekeeping good.

3. Printing shop - two printing machines; exposures to MEK, MIBK, toluene, inks; ventilation inadequate; men eat on the job; sanitary facilities not immediately available; housekeeping good.
4. Scrub reclaiming room - exposure to DOP; men working between exposure and hood; housekeeping good.
5. Film and leather room combined - two calendars and two forming ovens; exposures and work practices as in No. 1 and No. 2 above; housekeeping good.
6. Extruder plant - extruders, bagging operations, gas powered fork lifts, exposures to pigments, PVC, stabilizer dusts and carbon monoxide; ventilation inadequate at bagging operation; men eat on the job; sanitary facilities not immediately available; workers with dusts wear masks and are required to have frequent haircuts and shampoos; many workers wear cotton gloves to prevent burns; housekeeping fair.
7. Machine shop - welding; ventilation probably adequate; protective equipment available; housekeeping fair.
8. Laboratory - usual laboratory procedures; small extruder; approximately 30 employees; one hood available; one bottle of MBK seen; Coleman mercury analyzer equipment; housekeeping good.
9. Master batch room - make color chips; exposures to color dyes, stabilizer dusts; men work between exposure and ventilation equipment; protective masks and cloth gloves normally worn; housekeeping good.
10. Catalyst building - has an enclosed room under negative pressure for handling toxic substances; exposures to sulfuric acid, chromic acid, sodium cyanide, hydrogen cyanide; well ventilated plus scrubber; at one time had a bird in room to detect toxic levels of gases; protection equipment available including gas masks and clothing; housekeeping good.
11. Dry chlorine unit - not operating on visit; make HCl and send to TVCM plant; exposures to noise, ear plugs required; housekeeping good.
12. Chlor-alkali plant - 31 mercury cells plus 5 under construction; each cell opened for 5 hours and cleaned once monthly; exposure principally to mercury which is purchased in 70 pound metal containers from U. S. and Mexico; 5 men on 3 shifts after new

cells completed; ventilation inadequate, particularly in view of new installation; sanitary facilities available but inadequate; (men are supposedly required to shower daily but a single shower beneath cells is nearly inaccessible) workers mainly stand around inside perimeter of building and upwind to reduce exposures; housekeeping fair (some mercury was observed on the cement floor beneath the cells); vacuum equipment is available and working to clean mercury spills.

13. Soda flake operation - beneath mercury cells; exposure to soda flake and mercury; ventilation and lighting inadequate; protective equipment available.
14. Drying plant - drying and bagging operations; bags are heat-sealed; exposure to PVC resin; ventilation inadequate; men wear masks.
15. Autoclave building - 12 reactors; exposures to VCM and PVC flake (during normal operations the cleaning inside the reactor takes 3 men about 1 hour, 4 reactors per shift); ventilation inadequate; shorts only normally worn to clean reactors (no gloves or shoes); no respiratory protective equipment.
16. Pilot plant - one small reactor for polymerization; when operating one reactor cleaner/shift required; exposures to VCM, PVC, ethyl acetate, maleic anhydride, lauryl peroxide; ventilation by two elevated fans inadequate; sanitary facilities not immediately available; housekeeping fair.
17. VCM unit - carbide process; exposure to VCM with leaks and when lab samples are taken or when residue is discharged from distillation; ventilation normally good since unit is outdoors; protective equipment available; housekeeping good.
18. Asbestos from Taiwan was used in the manufacture of floor tile in the Toufen factory for 2 years until 2 years ago. Normally asbestos is not used as an insulation material in this factory.
19. All factory water is supplied from deep wells on-site and is treated chemically and by aeration. It is checked periodically for chemical content but not for bacteria. The Chinese, however, customarily boil all water before using for food or drink. Sewage is discharged directly into the Chungkang River 4 kilometers from the factory without treatment.

Industrial effluent treatment facilities are presently under consideration. Industrial waste is discharged directly into the river except for the carbide slurry which is neutralized in a holding pond on-site. I was told that government regulations now requiring a limit of 200 grams/metric ton of NaOH will decrease to 100 grams/metric ton in 1975 and probably lower thereafter. About \$NT 300,000 (\$U.S. 7,916) is paid yearly to local farmers to compensate for crop damage.

TAOYUAN PLANT

The Taoyuan Plant of CGPC is located in the countryside about 8 kilometers from the town of Taoyuan and 30 kilometers from Taipei. Mr. P. C. Parng is plant manager. This plant which is a satellite of the Toufen Plant is two years old but was purchased by CGPC in May 1973. Personnel records are kept at Toufen.

There are 93 employees (13 staff including 2 women and 80 workers) on 3 shifts of 8 hours each, 7 days weekly (6 days weekly beginning April 1). Turnover is said to be high. A new dormitory is under construction which will accomodate more workers than the 16 presently living in the old unit. Salaries average \$NT 60 to \$NT 80 per day (\$U.S. 1.50-2.00) and benefits are similar to those previously described for the Toufen employees. All workers are issued 2 complete uniforms and one jacket per year and are responsible for laundering. Work practices are similar to the Toufen Factory and it is customary for the men to eat on the job.

The plant fabricates PVC film and sheet from PVC resin. Plasticizers (DOP), fillers (calcium carbonate), and stabilizers (lead, cadmium and barium stearate) are added to PVC resin in a high speed mixer and then gravity fed into a Bambuary mixer where color pigments (red, yellow, green, etc.) are added. The material then goes through a mixing roll (140°C.) to a strainer (PVC string), then to a calender (170°C.) and finally to cooling and winding drums. Finished products are shipped by outside trucking firms. Both calenders are usually operating but because of the lack of orders only one was in use during my visit. A laminating machine in the room was also not operating. Normally 6 men are required on the calender line per shift. In addition, each shift has a foreman, boiler man and electrician on duty. Maintenance is carried out by one man on the day shift only while workers are also responsible for cleaning their machines. There is a small one-man laboratory, a small repair shop where welding is done and the boilers are located in a separate building.

Workers who add materials to the mixers are primarily exposed to PVC resin and stabilizer dusts and wear cloth masks. Ventilation equipment is available near the point of dust generation but an exhaust had been detached. Both mixing rolls and calenders have large overhead exhausts but DOP was easily detectable close to the calender which was operating. Noise was not excessive with one line operating; however, boiler room workers may be exposed to excessive noise at times. Lighting was barely adequate

with all lights on. Housekeeping was very good. Sanitary facilities are immediately available near the operations area. A shower is supposedly available in the plant but was not observed.

All water for plant and personal use comes from a 300 foot well on-site. The water is filtered, goes through an ion exchanger and is aerated. Samples are tested every three months for minerals including iron and cadmium but no bacteria checks are made. Waste effluent is not treated and sewage goes by open trench to a nearby rice paddy.

Medical services are not available on-site and the plant minibus has not been adapted for stretchers. First aid kits are kept in the plant but are inadequately stocked. Supervisors receive a minimum of first aid training along with safety instruction. Accidents are few and generally are finger injuries in calender workers. Emergencies are sent by car or ambulance to a small hospital about 5 minutes from the plant or to St. Paul's Hospital in Taoyuan about 30 minutes away. Both facilities have been approved by the DOL to handle industrial cases.

All workers have preemployment examinations at DOL-approved facilities which include height, weight, blood pressure, chest and abdominal checks, serology, and chest fluoroscopy. Major reasons for rejection include a positive serology, tuberculosis and color blindness. Annual checks are similar and are also done outside the plant in government approved facilities except for a chest x-ray survey conducted by the government on-site.

KUEISHAN PLANT

This newly acquired plant of CGPC is located in an industrial complex near Taoyuan. Mr. Huang Pei Chia is plant manager. The plant is 6 years old and was purchased by CGPC in March, 1974. It is also called Waterfall Plastics Fabrication Ltd.

There are 175 employees (17 staff, 140 female workers, 18 male workers) on one shift, 6 days weekly or 13 days every 2 weeks. The women are quite young - minimum age of hiring without a permit is 16 and with a permit is 14 -- and turnover is very high. Women cannot work in a factory after 10 P.M. Quitting seasons are generally after the lunar New Year when bonuses are given and after general increases if inadequate. Nearly 80% of the women live in nearby Company dormitories. A newly hired female worker makes about \$NT 48/day (\$U.S. 1.27) plus \$NT 12/day (\$U.S. 0.32) meal allowance. Experienced women get about \$NT 60/day (\$U.S. 1.58). Benefits are as previously described except that the women receive 3 uniform issues/year (2 shirts and skirts and 1 jacket and pants). A laundry is available near the dormitories for their use.

This plant fabricates PVC film, sheet and leather into a wide variety of finished products including raincoats, shower curtains, mattress covers, shoe files and bags, steering wheel covers, pillow protectors, travel suit bags, curtains, purses, tote bags, table mats and air mattresses. Operations consist of cutting, sewing, high frequency welding, folding and packaging of the plastic materials and products. Women normally perform all of these activities except for cutting. High frequency welding is with a copper electrode and produces no discernable fume. The only odor in the plant is from the PVC plastic itself. There is no noise problem and lighting seems adequate. There is no air-conditioning in the factory and the main work area under a corrugated roof probably is very hot in the summer season.

Preemployment and periodic examinations are similar to those previously described and are done in the local hospitals and clinics. A small first aid unit is available in the industrial complex with a full-time physician, Dr. Chang, who normally handles very minor cases only and sends the rest to the local hospitals including Poai Hospital in Taoyuan. A minibus is used to transport patients and an ambulance may be called from St. Paul's Hospital although this has not been necessary to date. No one has received first aid training.

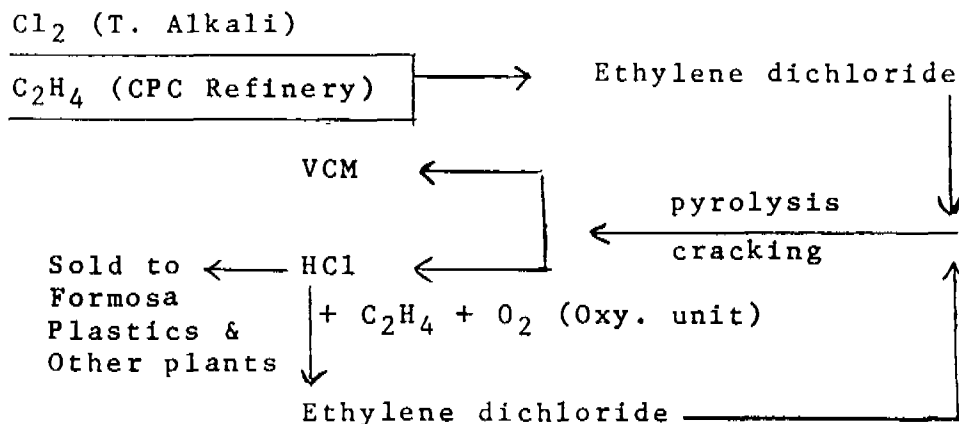
TAIWAN VCM INDUSTRIAL CORPORATION

KAOHSIUNG PLANT

This plant which is located in the city of Kaohsiung was built by Taiwan Alkali Corporation and began operation in April 1971. CGPC now owns a minority interest but maintains management control. The manager is Mr. Chow Tsung Lin. The plant sits at the periphery of the large Taiwan Alkali Corporation facility and near a large Formosa Plastics factory.

There are presently 156 employees (5 female) working 3 shifts, 8 hours daily, seven days a week. In the past there has been a tendency to rotate jobs. Employment will increase by 9 or 10 persons when the new oxy unit now under construction is on stream. About 1/2 of the personnel are Taiwan Alkali employees and there is evidently some uncertainty about their employment status since the CGPC intervention. This also applies to the benefit program. There is a dormitory nearby for some of the workers. Uniforms have not been issued yet but one is ready. Most workers carry a lunch box and eat on the job although there is a private cafeteria across the street. Each worker has a small locker and shower facilities are available near the plant entrance but look little used and were not all functioning properly.

Production was 120 metric tons VCM/day although the plant was designed for 180 metric tons/day. The VCM process is simply shown as follows:



The process is enclosed and outdoors. Chlorine, ethylene dichloride and vinyl chloride are commonly smelled out in the plant. Vinyl chloride exposures occur primarily with

leaks and when sampling for laboratory analyses. Freon gas is used as a refrigerant. The oxy unit is under construction and should be on stream this July. The plant is run from a large enclosed control room. A product pipeline runs from the plant to the dock (Kaohsiung is the second largest seaport in Taiwan). The compressor for the refrigerant was noisy. Housekeeping was fairly good.

The plant does not have its own medical facility but still relies on the Taiwan Alkali first aid unit which now has a part-time doctor on-site. It is uncertain whether they will be able to continue to use this as a medical backup.

TAIWAN VCM INDUSTRIAL CORPORATION

TOUFEN PLANT

This plant which also manufactures VCM is across the road from the main CGPC Factory near Toufen. The plant is new and began operations in April, 1974. Production will approximate 5,000 metric tons/month. It is adjacent to a China Petroleum Company (CPC) ethylene plant from which ethylene is piped directly to TVCM.

Since the plant manager, Mr. C. C. Young, was not present on the day of my visit, I was escorted through the plant by Mr. Wilbur Shyeh and Mr. T. H. Wei, Superintendent of Operations.

There are 74 employees (19 staff and office, 30 operators, 18 maintenance, 7 laboratory) working 3 shifts, 8 hours daily and seven days a week. Many of the workers have been assigned from the CGPC Toufen plant. Benefits presumably will be similar to those offered the Toufen factory workers. The Toufen dormitory is also available to these workers. Each man has a locker and uniforms. Wash facilities are available but there are no showers.

The process is similar to that described for the TVCM plant in Kaoshiung. During start-up several leaks were identified and the odor of ethylene dichloride was evident in several areas. New asbestos insulating material was seen in one location. Propylene and methanol are used as a refrigerant and coolant, respectively. A bomb sample of VCM is taken at least once daily for laboratory analysis. A Japanese cannister mask with halogen filters is used for this purpose. Tar (heavy ends) are removed from one of the units daily by lifting a bucket from a filter. The tar is then allowed to weather on the property (presumably this activity also takes place in Kaoshiung.) To date one worker assigned to this plant from the main Toufen plant complained of an allergy to the vapors and has been re-assigned. Several workers have indicated a dislike for the odor of ethylene dichloride.

Only those workers transferred from the main Toufen plant have had physical examinations as part of the CGPC program. The new hires have not been sent for medical evaluation as yet. The nearest medical facility is at the main Toufen plant and I understand will be available, presumably on a limited basis, to these workers. Otherwise the local

hospitals and clinics in Toufen are used for emergency cases. There is no ambulance or vehicle suitable for stretcher cases on site. First aid training has not been given.

Water comes from the Toufen city water supply or from a deep well at CPC. Industrial waste goes to the main Toufen plant holding pond for neutralization with the carbide slurry and then to the river. Raw sewage is piped directly to the river.

CONCLUSIONS

Medical Considerations

1. Although no clinical cases of acute or chronic toxicity have been identified, including acroosteolysis and liver cancer, in the workers exposed to VCM, PVC, solvents, mercury stabilizers, pigments and DOP, there have been numerous complaints of headaches, solvent odors and dusts and an absentee survey suggests that solvent and VCM workers have more absences than other groups.
2. Records of sickness absence are inadequate to define problem areas within the factories.
3. Medical personnel, facilities and equipment at the Toufen Factory are inadequate to carry out an effective preventive medicine program. There is no on-site medical service at the other factory locations with the exception of the Kaohsiung and Waterfall plants where first-aid units staffed by physicians are available nearby and may be used by CGPC employees at this time.
4. The handling of emergency cases is limited by the general lack of 1) first-aid equipment on-site, 2) trained first-aiders and 3) vehicles capable of carrying stretcher cases.
5. The oxygen inhalation equipment in the Medical Department at the Toufen Factory is inadequate for emergency resuscitation and aspiration.
6. There are no occupational health physicians or industrial hygienists in Taiwan. At this time there is a major effort underway to establish a center for occupational health consulting services at the University of Taiwan, College of Medicine. Industry will be asked to participate. Two Chinese engineers sponsored by Philco are presently in a one-year course at the University of Washington in Seattle.
7. The DOL in Taiwan plays a similar role to the U. S. Department of Labor by conducting factory inspections and recommending engineering controls and medical surveillance procedures. As in the U. S. the staff is too small and inadequately trained to carry out its functions and assure compliance. Nevertheless, they have visited the Toufen Factory. In addition, they have been known to make extensive and costly recommendations without supportive data.

8. A new occupational health law more restrictive than the U.S. OSHA regulations was passed by the legislation in April, 1970. It places the responsibility for health and safety directly in the hands of the factory manager or owner and specifies severe penalties, including prison sentences, for non-compliance.
9. Liver disease, specifically primary hepatoma, is very common in the Chinese population. Acute infectious hepatitis is uncommon in the adult; however, 20 percent are positive reactors to hepatitis B antigen.
10. The quality of laboratory services in Taiwan is highly variable. The laboratory presently being used in Toufen is inadequate. Local authorities seem to agree that the most reliable laboratory facilities in order of preference are the 1) Veterans General Hospital, 2) Taiwan University Hospital, 3) NAMRU-2 (not able to accept specimens from private agencies at this time), 4) U. S. Navy Hospital, 5) Private hospitals, 6) Private clinics (not recommended). Blood and urine lead and urine mercury analyses cannot be accurately done in Taiwan although NAMRU and the U. S. Navy Hospital have performed lead analyses in the past.

Industrial Hygiene and Toxicological Considerations

1. Many workers are being exposed to concentrations of solvents, mercury, stabilizers and VCM which exceed presently accepted (1973) U. S. Threshold Limit Values (TLV). These values which follow refer to time-weighted concentrations for an 8-hour workday and 40-hour workweek. Since CGPC workers normally work a 48 or even 56 hour workweek their TLV's must be correspondingly lower.

TLV (U.S.)

MEK	200 ppm.	
MIBK	100 ppm.	
Toluene	100 ppm.	(200 c)
Mercury	0.05 mg./m ³	(proposed)
Lead stearate	0.15 mg./m ³	(for lead)
Cadmium stearate	0.2 mg./m ³	(for cadmium)
Barium stearate	0.5 mg./m ³	(for barium)
VCM	50 ppm. (c)	(temporary standard)

2. Solvent, mercury and stabilizer exposures are of greater immediate concern than VCM or PVC exposures because of their greater potential for serious acute effects; however, the carcinogen potential of VCM is the overriding issue of the moment and will largely dictate the control measures.
3. Environmental monitoring has been sporadic and inadequate and equipment is not available on-site to assess the potentially hazardous exposures accurately.
4. Two CGPC employees in Toufen have been instructed in the sampling procedures and the use of the equipment to be purchased but neither employee has any experience or training in industrial hygiene.
5. Hygiene facilities and work practices in the factories are generally poor or unsatisfactory. Most factory workers eat on the job and lunchrooms are not available in all the factories. Handwashing basins are often inconvenient and in many areas are outdoors. Showers are very limited or non-existent and in some instances are poorly located. Locker and change room facilities are variable but generally inadequate. There are no set procedures for changing and laundering uniforms and, except for the mercury-exposed group, it is customary to wear work clothes home.
6. There appears to be unrestricted access to most operations including areas of potential exposure to VCM and PVC.
7. Noise is not a major problem in the factories although there are some jobs, e.g. boiler room workers, workers near the chlorine compressor, workers around refrigeration equipment and possibly others, who appear to be exposed to noise in excess of recommended levels.
8. Bacteriological analyses of "potable" water supplies is not done at any of the factory locations.
9. Sanitary wastewater receives no treatment at any factory location and industrial wastewater treatment is limited only to neutralization of the carbide slurry and the TVCM effluent in a holding pond at the Toufen Factory. Measurable mercury levels are found in the effluent and annual payments are made to local farmers. This presents a serious potential health problem which is presently under consideration by CGPC. Local regulations are evidently becoming more restrictive and will necessitate action by CGPC in the near future.

10. Lighting in the factories is variable and in some operations, i.e. soda flake area, is insufficient. All lights in most areas were turned on during my visit. which may not reflect the usual situation in view of the current energy crisis cutbacks.

REFERENCES

1. Newspaper articles
2. Kentucky Vinyl Chloride Standard
3. NIOSH Recommends Zero Threshold for Vinyl Chloride
4. NIOSH recommendations for Work Practices and Medical Surveillance of VCM and PVC Workers
5. OSHA Emergency Temporary Standard on Vinyl Chloride
6. National Surveillance Registry
7. Kodakisa Report on MBK
8. Health Hazard Evaluation of Meat Wrapping Employees
9. Markowitz, S. S., et al. Occupational Acroosteolysis. Archives Dermatology, Vol. 106, August 1972
10. Getsios, C. T. Acroosteolysis in PVC Workers. Presented at the Sixth European Medical Directors Meeting, Standard Oil Company; (N.J.), Paris, France, 1970
11. Yagaguchi, S., et al. Occurrence of Alkylmercury Compound in Caustic Soda Factory. Archives Environmental Health, Vol. 23, September 1971
12. Viola, P. L. Pathology of Vinyl Chloride. Medicina del Lavoro, Vol. 61, March 1970
13. Viola, P. L. Cancerogenic Effect of Vinyl Chloride. Presented at the Tenth International Cancer Congress, Houston, Texas, May, 1970

Wall Street Journal, Thursday, January 24, 1974

Three Cancer Deaths May Be Job-Related, B. F. Goodrich Says

Former Employees at Louisville
Plant All Were Involved in
Polyvinyl Chloride Operation

By a WALL STREET JOURNAL Staff Reporter

AKRON, Ohio -- B. F. Goodrich Co., in a move that sent ripples through the plastics and chemicals industries, said it is investigating the possibility that the cancer deaths of three workers at a plant in Louisville, Ky., may be job-related.

Goodrich said that the workers affected were in its polyvinyl chloride operations, and that they died of angiosarcoma of the liver, a rare form of liver cancer.

Dr. Maurice N. Johnson, Goodrich's director of environmental health, said in the company's statement that he had recently received medical reports concerning the death of an employee in late December. "A review of medical records uncovered that two other employees had apparently died from the same cause—one in September 1971 and one in March 1973," the company said.

It was understood that a fourth death—in 1968—involving a more common form of liver cancer was considered outside the reasonable bounds of the "grouping" of the three recent deaths, all attributed to angiosarcoma.

Goodrich said it had informed Kentucky health officials and the Federal National Institute of Occupational Safety and Health that the company was investigating the possibility that the deaths might be "related to occupational causes."

Will Begin Investigation

Kentucky officials said they had just learned of the situation at the Louisville plant and had asked a medical expert to investigate. In Rockville, Md., a spokesman for NIOSH said a team of experts will arrive in Louisville this morning to begin an investigation.

Dr. Marcus M. Key, director of NIOSH, said the institute also will step up efforts to determine the extent of angiosarcoma in the U.S., and in foreign countries with similar manufacturing processes. A spokesman for the institute said the best information available shows 21 deaths per year in the U.S. attributable to angiosarcoma.

The recent deaths at Louisville, according to Dr. Johnson of Goodrich, involved workers in the company's vinyl products operations. An official of NIOSH said he understood that the workers had an average of 20 years' exposure to various chemicals and agents involved in vinyl operations.

Goodrich said it has been conducting a program to reduce exposure to hydrocarbons, particularly vinyl chloride, throughout its operations. Further steps to limit exposure and to describe the situation to workers in vinyl products production are being taken, the company said.

Goodrich also said it is providing medical examinations to all employees involved in any phase of vinyl chloride or polyvinyl chloride production, and is reviewing all its medical records of former or retired employees.

About 1,200 persons work at the Louisville plant, of whom about 270 are involved in vinyl products operations.

"Dropping of a Bomb"

Word that the deaths might be job-related spread quickly throughout several industries. Said Louis Beliczky, an industrial hygienist on the staff of the United Rubber Workers union, which has many members involved in vinyl operations at various companies: "I look at this as the dropping of a bomb. It opens up the possibility of a whole new occupational disease."

Mr. Beliczky said he suspected there might be a connection between the Goodrich problems at the Louisville plant and the problems of Borden Inc. at a vinyl-materials plant in Columbus, Ohio. Workers at the Borden plant for several months have complained of a variety of ailments, some believed crippling, which they allege are connected with working conditions.

A medical expert at NIOSH, however, said he doubted the difficulties at the two plants were related. He asserted that the problem at the Borden plant has been defined as peripheral neuropathy, a disease that attacks nerves that control muscles in human limbs. The liver afflictions at the Goodrich plant seem unrelated to the problem at Borden, he said.

Goodrich has four other polyvinyl chloride plants—at Avon Lake, Ohio; Calvert City, Ky.; Long Beach, Calif.; and Henry, Ill.

R.1
Saturday, Jan. 26, 1974

THE WASHINGTON POST

Liver Cancer Cases Spur Plant Inquiry

By Stuart Auerbach
Washington Post Staff Writer

Deaths from a rare form of liver cancer of three workers in a Louisville plastics plant has led to a federal investigation to see if they were caused by the chemicals used in the plant.

All three men were long-time workers in a B. F. Goodrich plant that makes polyvinyl chloride—a plastic used in phonograph records, pipes for the construction industry, bottles, packaging, car upholstery and vinyl tops for automobiles.

The men died of angiosarcoma, a form of liver cancer that kills about 23 Americans a year. Two of the men died last year, in March and in December, and the third died in September, 1971.

"Certainly two deaths in one year in the same plant, among co-workers almost; out of 23 in the entire United States is enough to heighten suspicion that chemicals in the plant caused the deaths," said Dr. Vernon Rose of the National Institute of Occupational Safety and Health, who returned yesterday from an inspection of the Louisville plant.

B. F. Goodrich said in a press release that it was investigating to see if the deaths "were related to occupational causes."

The deaths caught experts in occupational health hazards by surprise. One man said that polyvinyl chloride had not been thought of as a cancer-causing agent and was not even on lists of chemical compounds that should be studied for their possible cancer-causing effects.

Although vinyl chloride, normally a colorless gas, is the main component of the plastic polyvinyl chloride, about 50 other chemicals are used in the plant. Company officials provided the federal investigators with a two-page list of chemicals that could be involved in the deaths.

"There is no question," said Rose, "as to the fact that the exposure to chemicals are numerous."

The company's own investigation started last week when Dr. Maurice N. Johnson, B.F. Goodrich's director of environmental health, received an autopsy report on the man who died in December.

This report had been furnished to the plant physician in Louisville, Dr. John Creech, by members of the worker's family.

Deaths from liver diseases are always considered suspicious in the chemical industry, B.F. Goodrich spokesman John Bell explained, because of the danger of exposure to unusual concentrations of hydrocarbons.

Johnson checked the medical records of other employees in the Louisville plant and found that two other men were reported as dying of angiosarcoma. The three men had an average of 22 years exposure to chemicals working in the plant.

In addition, Rose said, a fourth employee was reported as having died of an unspecified form of liver cancer.

Federal officials are now seeking to confirm the causes of death of all four men.

"There is no knowledge or record of any similar circumstances among the four other B. F. Goodrich polyvinyl chloride plants," said Bell.

Nevertheless, the company said it has tightened its safety standards to minimize employee exposure to the chemicals. Company officials said all five plants are operating within federally approved levels.

Rose said that federal experts will spend the weekend finding better ways to keep the plant, which was built in the 1930s, from being contaminated by chemicals.

CUSAROSS 00247

More Cases of Liver Cancer Are Reported Among Workers at Vinyl Chloride Plant

By JONATHAN SPIVAK
Staff Reporter of THE WALL STREET JOURNAL

WASHINGTON — Scientific evidence is mounting that the widely used industrial chemical vinyl chloride causes cancer in workers exposed to it.

The public health and industrial implications are serious and substantial, government experts say. "We are faced with a new occupational disease. There is no sense denying it," states John O'Neill, chief of the division of health standards in the Occupational Safety and Health Administration.

The evidence of vinyl chloride's hazards means a major change in manufacturing practices will be necessary to reduce workers' exposure to it. Federal and private industry experts are working on a high-priority effort to determine the exact extent of risk from the substance and what further precautions will be needed.

Vinyl chloride is used in making a wide array of plastics, including pipes, floor tiles, records and other consumer products. It normally is a gas and is converted in manufacturing to a material called polyvinyl chloride, a powdery substance that is then converted into finished products.

The first firm indications of the chemical's possible danger came last month with the report by B. F. Goodrich Chemical Co., a division of B. F. Goodrich Co., that it had been determined that four workers at its Louisville, Ky., plant, which converts vinyl chloride into polyvinyl chloride, had died from a rare type of liver cancer called angiosarcoma. This cancer, which affects the blood vessels of the liver, is thought to occur among only 25 persons a year nationwide. Thus, the cluster at the Goodrich plant, the largest manufacturer of polyvinyl chloride in the nation, stirred immediate concern.

Then, over the weekend federal authorities reported two more cases of angiosarcoma at the Goodrich plant, bringing to six the number occurring there. "This makes it a bigger problem than we had believed," declared Marcus Key, director of the National Institute for Occupational Safety and Health, which makes scientific recommendations to the Labor Department. The institute is part of the Health, Education and Welfare Department.

So far, however, federal authorities aren't prepared to assert specifically that vinyl chloride causes liver cancer. They note, along with Goodrich officials, that workers at the company's plant are exposed to a variety of other chemicals involved in the conversion of vinyl chloride to polyvinyl chloride. But the circumstantial evidence is increasing, and a strong case is building from records of human cancer and animal experiments that a substantial health problem has been uncovered.

The immediate issue is what new precautionary measures should be taken to protect workers. Some 6,500 employees at 37 plants operated by 23 U.S. manufacturers are involved. Union representatives have urged the Occupational Safety Agency to issue an immediate order tightening its existing limit of 500 parts per million in the atmosphere. Industry representatives, however, urge that the Labor Department take more time in investigating the problem and issue its new regulations under usual procedures, which permit a public hearing before they go into effect.

Alexander Reis, an official of the Occupational Safety Agency, said the decision on emergency regulations would be made only after additional information from current government and industry studies was available. "About the only thing that is clear is the existing standard will have to be changed," Mr. Reis said.

The HEW institute is urging that the Labor Department act as promptly as possible by issuing rules requiring vinyl chloride manufacturers to operate under a so-called "closed system." This means that workers would be fully protected against any exposure to the chemical, and it would require significant changes in manufacturing processes, government specialists say. The HEW recommendations also would call for monitoring of the environment in the plants and medical tests of workers to determine whether they are beginning to experience adverse effects. The institute also is urging that there be warning placards in manufacturing areas and that employers be required to provide specific warning information to employees.

Meanwhile, government and industry are accelerating efforts to determine the extent of the problem and to determine more definitively the role played by vinyl chloride in its cause. The Goodrich Louisville plant was one of the first to begin production of the plastic component after World War II and the type of cancer diagnosed in its employees is one that takes many years to become evident. The first four workers reported to have the disease had been exposed for at least 14 years before the illness.

An initial government step will be to survey other vinyl chloride plants, particularly those involved in conversion of vinyl chloride to polyvinyl chloride. A cluster of such plants occur in Ohio, Kentucky and Pennsylvania.

In addition, government specialists point out that an examination should be made of consumers' exposure through the use of products containing polyvinyl chloride, although there currently isn't any evidence of risk in this area. "We are talking about levels (of exposure) at present that are achieved only in the industrial environment," points out Dr. Clark Heath, chief of the cancer and birth defects division at HEW's Center for Disease Control.

The Wall Street Journal
Tuesday, February 19, 1974

CUSAROSS 00248

THE CHINA NEWS

TAIWAN

Vinyl Chloride May Cause Liver Cancer

ST. AUGUSTINE, Florida—(UPI)—Researchers warned Friday that a recent discovery that vinyl chloride may cause liver cancer among chemical workers suggests that other substances eaten and inhaled by humans may also produce cancer.

Drs. E. Cuyler Hammond of the American Cancer Society and Irving Selikoff of the Mount Sinai School of Medicine in New York said there is an urgent need to search for agents which may be causing cancers that will show up years from now.

"Our world is changing and, especially in the past 40 years, the environment in which we live has been altered to an extraordinary extent," they said in a paper prepared for a scientists' writers seminar sponsored by the cancer society.

"The air we breathe contains gases and particles that never before entered the human lung. Our food has chemicals designed to improve its taste, freshness, appearance, but which are strange to our intestines, livers, kidneys, blood. We touch, inhale, absorb an ever-increasing number of synthetic materials and, in other circumstances, agents which may have existed on earth but were never part of the immediate human environment."

Hammond and Selikoff pointed out that it is believed 85 per cent of all cancer is derived from environmental sources. They said new agents are rapidly being spread among tens of millions of people without pre-testing to see if they cause cancer or other diseases.

"A useful chemical or an efficient plastic soon permeates a nation, or large part of the world. There is literally no place to hide."

The vinyl chloride problem surfaced in January when officials of the B.F. Goodrich Co. in

Louisville, Kentucky, reported two fatal liver cancers among workers at the company's vinyl chloride plant. Five more cases were found at the plant and since then other cases have been found among vinyl workers in New York, Texas and West Virginia.

That type of cancer had been rare and Hammond and Selikoff said it was only because of its rarity that the vinyl chloride link was found. An American cancer society research project is now trying to determine if workers in factories which manufacture vinyl plastics are endangered, or if consumer products containing traces of vinyl chloride are hazardous.

Kentucky**STATE STANDARDS BOARD ADOPTS 50 PPM
TWA FOR POLYVINYL CHLORIDE STANDARD**

Kentucky's standards board amended the state's permanent carcinogens standard on February 19 to include a 50 parts per million limit of polyvinyl chlorides in air as a time-weighted-average (TWA), Labor Commissioner James Yokom, told OSHR.

The board adopted the TWA at an emergency meeting held following the deaths of workers at the B.F. Goodrich plant in Louisville, Ky., from angiosarcoma of the liver, a cancer attributed to exposure to vinyl chlorides during a polymerization process (Current Report, February 14, p. 1164).

The amended standard will become effective 30 days after filed, Yokom added. It is currently being reviewed by the state Legislative Research Commission as a matter of procedure and will be filed shortly.

In addition to the 50 ppm TWA, a ceiling value of 75 ppm for 15 minutes of worker exposure was established by the standard. Workers cannot be exposed to more than 75 ppm of vinyl chlorides for more than 15 minutes at a time without use of protective equipment, according to the amended standard. Protective equipment required, medical checkups, and recordkeeping, for polyvinyl chloride exposure is the same as required for other carcinogens under the state standard.

The standard also sets a value of 200 ppm without use of protective equipment to be considered and treated as an imminent danger situation, Yokom said.

The standard will require all companies using the chemical in the state to register with the state labor department by July 13. Under the carcinogens standard, the first 13 carcinogens must be registered with the state by June 13 at the latest.

Health Hazards

NIOSH RECOMMENDS WORK PRACTICES DOCUMENT FOR VINYL CHLORIDE WORK

Any employee exposed to measurable amounts of vinyl chloride should be required to wear an air-supplied respirator, according to a recommended standard for manufacture of synthetic polymer from vinyl chloride developed by the National Institute for Occupational Safety and Health.

The NIOSH document was sent to the Occupational Safety and Health Administration on March 11 by Dr. Marcus Key, NIOSH director. The document was prepared following the industry-wide scare that resulted from the announcement that several workers at the B.F. Goodrich facility in Louisville, Ky., had died from angiosarcoma of the liver, an extremely rare disease (Current Report, January 31, p. 1099).

In a memo to Assistant Labor Secretary John H. Stender, Key said the consultants from industry who worked with NIOSH on the standard recommended the rule contain the concept of an allowable working level for vinyl chloride gas in the atmosphere, which the consultants identified as a time weighted average of 50 parts per million. The consultants recommended that where workers were exposed to concentrations in excess of this level they be required to wear respirators.

The concept of an allowable "working level" might seem justifiable in that the Italian researcher Professor Maltoni found no liver tumors at 50 ppm, Key said (Current Report, February 21, p. 1189). However, 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, Key said. "In view of these considerations and our inability to describe a safe exposure level as required in Section 20(a) (3) of the Occupational Safety and Health Act, we rejected the concept of a threshold limit for vinyl chloride gas in the atmosphere."

Consequently, the NIOSH recommendations as contained in the recommended standard 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, Key said. This recommendation is based on some preliminary information that the standard chemical cartridge respirators are inefficient in protecting against vinyl chloride. NIOSH is conducting 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, Key said. 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.

The NIOSH recommendations for a standard for vinyl chloride appear in the Full Text section of this report.

R.

h. 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 non-hepatic health conditions potentially related to vinyl chloride monomer exposure. Routine health screening should include at 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 followup 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 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.

(i) At time of initial employment, or upon institution of screening, physical examination shall be performed with specific attention to detecting enlargement of liver or spleen by abdominal palpation.

(ii) At time of initial employment, or upon institution of screening and annually thereafter, a medical history check-list shall be completed by the employee. This list shall include questions concerning:

- (a) alcohol intake
- (b) past history of hepatitis
- (c) past exposure to potential hepatotoxic agents, including drugs and chemicals.
- (d) past history of blood transfusions
- (e) past history of hospitalizations

Completed medical check-lists shall be reviewed by a physician and should be acted upon as medically indicated for each individual employee.

(iii) At time of initial employment, or upon institution of screening, a serum specimen shall be obtained for screening with respect to the following five bio-chemical determinations of liver function:

- (a) total bilirubin
- (b) alkaline phosphatase
- (c) serum glutamic oxalacetic transaminase (SGOT)
- (d) serum glutamic pyruvic transaminase (SGPT)
- (e) gamma glutamyl transpeptidase (GGTP)

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 analyses 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.

(iv) If 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.

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

(vi) If abnormalities persist on rescreening, the employee shall be removed from contact with vinyl chloride monomer operations and individualized medical workup shall be instituted. Suggested as initial steps in medical workup 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.

(viii) 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.

NIOSH RECOMMENDED OCCUPATIONAL HEALTH STANDARD FOR THE MANUFACTURE OF SYNTHETIC POLYMER FROM VINYL CHLORIDE

March 11, 1974

1. SCOPE AND APPLICATION

This standard regulates the manufacture of synthetic polymer from vinyl chloride (chloroethene, Chemical Abstracts Registry No. 75014), in order to protect the health and safety of workers.

Vinyl chloride also known as vinyl chloride monomer (VCM), chloroethylene and chloroethene, is a colorless sweet smelling gas at ordinary temperature and pressure and has a boiling and melting point at one atmosphere of -13.8 degrees C. and -153.71 degrees C, respectively. Its chemical formula is CH_2CHCl and it has a molecular weight of 62.50. Although noncorrosive at normal atmospheric temperatures, in contact with water and at elevated temperatures it accelerates the corrosion of iron and steel. Of considerable concern is the fact that vinyl chloride is easily ignited and has a lower and upper explosive limit of 3.6 percent and 26.4 percent, respectively.

2. DEFINITIONS

For the purpose of this standard:

a. "Assistant Secretary" means the Assistant Secretary for Occupational Safety and Health, U.S. Department of Labor or any person directed by him.

b. "Director" means the Director, National Institute for Occupational Safety and Health, or any person directed by him or the Secretary of Health, Education, and Welfare to act for the Director.

c. "Authorized employee" means an employee whose duties require him to be in the regulated area and who has been specifically assigned by the employer.

d. "Detectable levels" means the determination that airborne concentrations of vinyl chloride are in excess of the limit of sensitivity of the sampling and analytical method recommended by the Director.

e. "Clean change room" means a room where employees put on clean clothing; clean change room shall be contiguous to and have an entry from a shower room, when the shower room facilities are otherwise required in this standard.

f. "Closed container" is any container which is used to prevent the physical contact of employees with material containing vinyl chloride monomer.

g. "Closed system" means an operation involving vinyl chloride where containment prevents the release of vinyl chloride into regulated areas, nonregulated areas, or the external environment.

h. "Contaminated" refers to detectable levels of vinyl chloride monomer.

i. "Decontamination" means the inactivation of vinyl chloride to less than detectable levels or its safe disposal.

j. "Disposal" means the safe removal of vinyl chloride from the work environment.

k. "Emergency" means an unforeseen circumstance or set of circumstances, such as a ruptured transfer line, resulting in the release of vinyl chloride sufficient to

produce acute symptoms among workers exposed or having contact with the vinyl chloride.

l. "External environment" means any environment external to regulated and nonregulated areas.

m. "Regulated area" means an area where entry to and exit from a vinyl chloride workplace is restricted and controlled.

n. "Nonregulated area" means any area under the control of the employer where entry and exit is neither restricted nor controlled.

o. "Protective clothing" means clothing designed to protect an employee against contact with or exposure to vinyl chloride.

p. "Waste resin" means any resin or other vinyl chloride reaction product which has been removed from vessels during clean-up operations, or which has been collected as a result of in-plant housekeeping operations.

3. REQUIREMENTS FOR REGULATED AREAS

A regulated area shall be established where synthetic resins containing vinyl chloride are manufactured. These regulated areas shall include but are not limited to vinyl chloride loading or unloading operations, storage, and transfer facilities; synthetic resin polymerization processes and operations; and resin handling, compounding, packaging and storage areas. Access shall be restricted to authorized employees only. All such regulated areas shall be controlled in accordance with the following requirements.

a. Routine Operations

(i) Initial concentration of vinyl chloride in all regulated areas shall be determined by performing air measurements at strategic sampling points under normal operating conditions. These initial sampling points must be selected by a professional industrial hygienist and will serve as monitoring locations for future environmental measurements.

The sampling pattern shall be adequate to represent the environment of the controlled area.

(ii) Where detectable levels of vinyl chloride are measured, a Control Plan to reduce such levels shall be developed and implemented. The Plan shall consist not only of establishing goals for reducing vinyl chloride levels by designing and introducing engineering and process controls, but shall also identify plans for developing additional (healthful) work practices. Target dates shall be established for all goals and the Plan must be updated at least on an annual basis. Copies of the Control Plan shall be posted in all regulated areas and be provided to all authorized employees.

(iii) There shall be periodic tests for process or equipment leaks and for emission of vinyl chloride which may result from work practices. The frequency of these tests shall be such as to insure the integrity of equipment, adherence to proper work practices, and to determine achievement of the goals of the Control Plan. Tests shall be performed at each sampling point at least daily or

more frequently if concentrations of vinyl chloride are in excess of those established in the Plan. When such levels are exceeded, additional samples to identify sources of contamination shall be taken. Results of all such tests shall be made available to authorized employees in such a manner as to evaluate achievement of goals contained in the Control Plan.

(iv) 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, of the continuous flow or pressure demand type in accordance with §1910.134.

(v) In operations involving loading or unloading vinyl chloride monomer from tank cars, trucks, barges, or other conveyance equipment, each transfer line and each vapor-equalizing line shall be equipped with vent connections permitting, at the completion of the transfer, pressure to be vented and the hose purged with an inert gas in such a manner to preclude any employee exposure. Specific and detailed transfer procedures shall be developed and provided to involved employees in written form.

(vi) Employees shall be provided with and required to wear, clean, full-body protective clothing (smocks, coveralls, or long-sleeved shirt and pants), and gloves prior to entering the regulated area.

(vii) Prior to each exit from a regulated area, employees shall be required to remove and leave protective clothing and equipment at the point of exit and at the last exit of the day, to place used clothing and equipment in impervious containers at the point of exit for purposes of decontamination or disposal. The contents of such impervious containers shall be identified as required under paragraph c(2) (i) of this standard.

b. Reactor and Vessel Entry

(i) A reactor and vessel entry procedure shall be developed and provided to involved employees in written form. Employees shall be familiarized with the procedure and shall be trained and rehearsed in the techniques provided for in the procedure. Emphasis shall not only be placed on concern for potential exposure to vinyl chloride but shall also include appropriate precautions for entry into confined spaces.

(ii) Techniques shall be developed and applied to minimize to the maximal practicable extent employee exposure to vinyl chloride when opening any closed vessel. Examples of effective methods are the application of heat or suction to the vessel prior to opening, or use of sufficient exhaust ventilation around the vessel. Where operations such as cleaning or maintenance conducted inside an open vessel could result in the liberation of vinyl chloride, suitable procedures such as exhaust ventilation shall be developed and implemented to insure that vinyl chloride is not released into the general work environment.

(iii) Exhaust air shall not be discharged to regulated areas, nonregulated areas, or the external environment unless decontaminated.

(iv) All piping to and from the vessel shall be blanked or otherwise isolated prior to entry.

(v) Employees entering the reactor or vessel shall be provided with and required to wear and use a full-face,

supplied air respirator, of the continuous flow or pressure demand type in accordance with §1910.134.

(vi) Employees entering the reactor or vessel where levels of vinyl chloride are monitored and are found to not exceed ambient levels external to the vessel shall be provided with and required to wear clean, full body protective clothing (coveralls or long-sleeved shirt and pants), gloves, footwear or foot coverings, and head covering. Where vessel levels are in excess of ambient levels, employees shall instead be provided with and required to wear impervious clothing to prevent skin contact of vinyl chloride or other materials containing vinyl chloride.

(vii) After each exit from the reactor or vessel, employees shall be required to remove and leave protective clothing and equipment at a designated point in the regulated area, and at the end of each work shift to place used clothing and equipment in impervious but vented containers for the purpose of decontamination or disposal. The contents of such impervious containers shall be identified as required under paragraph c(2) (i) of this standard.

(viii) Employees engaged in reactor cleaning or other operations involving vessel entry shall shower at the end of the work shift.

c. Maintenance and Decontamination Activities

(i) Emphasis shall be placed upon immediate clean up of spills, periodic inspection, prompt repair of equipment and leaks, and proper handling, storage and disposal or decontamination of materials to prevent airborne contamination and accidental skin contact with vinyl chloride. Because vinyl chloride is a gas at normal temperatures, waste materials, equipment, and other sources of the monomer in closed containers, shall not be placed in areas of excessive temperature or sunlight since build-up of internal pressure may result in rupture of the container, fire or explosion.

(ii) Waste resins or other materials contaminated with vinyl chloride shall be placed in closed containers identified as required under paragraphs c(2) (i) or (ii) of this standard.

(iii) Appropriate procedures shall be developed and implemented for the decontamination and/or disposal of all such waste material.

(iv) In clean-up of leaks or spills, maintenance or repair operations on contaminated systems or equipment, or any operation involving work where direct contact with vinyl chloride monomer could result, each authorized employee involved in such operations shall be provided with and required to wear clean, impervious garments, including gloves, boots and continuous air supplied hoods in accordance with §1910.134, be decontaminated before removing the protective garments and hood; and be required to shower upon removing the protective garments and hood.

d. General Regulated Area Requirements

i. Employee Identification.

A daily roster of employees entering regulated areas shall be established and maintained. The rosters or a summary of the roster shall be retained for a minimum period of 20 years by the employer or successors thereto. The rosters and/or summaries shall be provided upon

request to authorized representatives of the Assistant Secretary and the Director. In the event that the employer ceases business without a successor, rosters shall be forwarded by registered mail to the Director.

2. Emergencies.

In an emergency, immediate measures including but not limited to the requirements of subdivisions (i), (ii), (iii), (iv), and (v) of this subparagraph shall be implemented.

(i) The potentially affected area shall be evacuated as soon as the existence of the emergency has been determined.

(ii) Hazardous conditions created by the emergency shall be eliminated and the potentially affected area shall be decontaminated prior to the resumption of normal operations.

(iii) Special medical surveillance by a physician shall be instituted within 24-hours for employees present in the potentially affected area at the time of the emergency. A report of the medical surveillance and any treatment shall be included in the incident report, in accordance with paragraph (g) (3) of this standard.

(iv) Where an employee has a known contact with liquid vinyl chloride such employee shall be required to shower as soon as possible, unless contraindicated by physical injuries.

(v) An incident report on the emergency shall be reported as provided in paragraph (g) (3) of this standard.

3. Hygienic facilities and practices.

(i) Storage or consumption of food, storage or use of containers of beverages, storage or application of cosmetics, smoking, storage of smoking materials, tobacco products or other products for chewing, or the chewing of such products, are prohibited in regulated areas.

(ii) Where employees wear protective clothing and equipment clean change rooms shall be provided, in accordance with §1910.141(c) (3).

(iii) Where employees are required by this standard to wash, washing facilities shall be provided in accordance with §1910.141(d) (1) and (2) (ii) through (vii).

(iv) Where employees are required by this standard to shower, shower facilities shall be provided in accordance with §1910.141(d) (3).

4. Contamination control.

(i) Regulated areas, except for outdoor systems, shall be maintained under negative pressure with respect to nonregulated areas. Local exhaust ventilation may be used to satisfy this requirement. Clean tempered makeup air shall replace air removed. Exhaust air shall not be discharged to regulated areas, nonregulated areas, or the external environment unless decontaminated.

(ii) Any equipment, material, or other item taken into or removed from a regulated area shall be done so in a manner that does not cause contamination in nonregulated areas or the external environment.

(iii) Decontamination procedures shall be established and implemented to remove vinyl chloride from the surfaces of materials, equipment and the decontamination facility.

c. Signs, Information, and Training

1. Signs.

(i) Entrances to regulated areas shall be posted with signs bearing the legend.

CANCER-SUSPECT AGENT AREA AUTHORIZED PERSONNEL ONLY

(ii) Entrances to regulated areas containing operations covered in paragraph 3(c) of this standard shall be posted with signs bearing the legend:

CANCER-SUSPECT AGENT IN THIS AREA. IMPERVIOUS SUIT INCLUDING GLOVES, BOOTS, AND AIR-SUPPLIED HOOD REQUIRED AT ALL TIMES. AUTHORIZED PERSONNEL ONLY.

2. Container contents identification.

(i) Containers of waste or other materials contaminated with vinyl chloride shall be labelled as follows:

**VINYL CHLORIDE CONTAMINATED MATERIAL
CANCER SUSPECT AGENT
DISPOSE OF OR DECONTAMINATE USING
APPROVED PROCEDURES**

(ii) Containers of synthetic polymers made from vinyl chloride shall be labelled as follows:

**SYNTHETIC VINYL CHLORIDE POLYMER
VINYL CHLORIDE IS A CANCER SUSPECT AGENT
POLYMER CONTAINS *% BY WEIGHT UNREACTED
VINYL CHLORIDE**

*(To be analytically determined by manufacturer and appropriate value entered on labels.)

(iii) Containers of vinyl chloride shall be labelled as follows:

**VINYL CHLORIDE
DANGER! EXTREMELY FLAMMABLE LIQUID AND
GAS UNDER PRESSURE
CANCER SUSPECT AGENT
HARMFUL IF INHALED
MAY POLYMERIZE VIOLENTLY
UNDER FIRE CONDITIONS
OR LOSS OR REMOVAL OF INHIBITOR**

Keep away from heat, sparks, and open flame.

Keep container closed.

Use with adequate ventilation.

Avoid breathing vapor.

Avoid contact with skin.

Keep cylinder out of sun and away from heat.

Container should be grounded when being emptied.

Never drop cylinder.

FIRST AID: If inhaled, remove to fresh air. If not breathing give artificial respiration, preferably mouth-to-mouth. If breathing is difficult, give oxygen. Call physician.

In case of:

Fire - Use water spray, dry chemical, or CO₂.

Spill or Leak For small spills, evacuate area and permit to evaporate. For large spills or leaks, evacuate area. Dike or flush to ground and let evaporate. Do not flush to sewer because of explosion hazard.

3. Training and indoctrination.

(i) Each employee, prior to being authorized to enter regulated area, shall receive a training and indoctrination program including, but not necessarily limited to:

(a) The nature of the carcinogenic hazards of vinyl chloride monomer, including local and systemic toxic.

(b) The specific nature of the operation involving vinyl chloride monomer which could result in exposure;

R. 4

(c) The purpose for and application of the medical surveillance program.

(d) The purpose for and application of decontamination practices and purposes.

(e) The purpose for and significance of emergency practices and procedures.

(f) The employee's specific role under normal operating or emergency conditions.

(g) Specific information to aid the employee in recognition and evaluation of conditions and situations which may result in the release of vinyl chloride monomer.

(h) The purpose for and application of specific first aid procedures and practices.

(i) A review of this standard at the employee's first training and indoctrination program and annually thereafter.

(ii) Specific emergency procedures shall be prescribed, and posted, and employees shall be familiarized with their terms, and rehearsed in their application.

(iii) All materials relating to the program shall be provided upon request to authorized representatives of the Assistant Secretary and the Director.

1. Environmental Monitoring and Recordkeeping

(i) Environmental concentrations of vinyl chloride shall be determined through the use of methods for sampling and analysis recommended by the Director or by methods of at least equal sensitivity.

(ii) Employees or their representatives shall be provided with the opportunity to observe environmental monitoring activities and shall have access to the results.

(iii) Complete and accurate records of all environmental measurements shall be maintained for at least 20 years by the employer or successors thereto and shall be provided upon request to authorized representatives of the Assistant Secretary or the Director.

2. Reports

1. Operations

Within 60 days the following information shall be reported in writing to the appropriate Occupational Safety and Health Administration (OSHA) Area Director.

Any change in such information shall be similarly reported within 15 calendar days of such change.

(i) A brief description and in-plant location of the area(s) regulated and the address of each regulated area.

(ii) The number of employees in each regulated area, during normal operations, including maintenance activity.

(iii) A copy of the Control Plan as developed under paragraph 3(a) (ii).

(2) Environmental Measurements

On a semi-annual basis the results of measurements taken at strategic sampling points, presented in such a manner as to identify achievement of goals established in the Control Plan, shall be reported in writing to the appropriate OSHA Area Director.

(3) Incidents

Incidents which result in the release of vinyl chloride monomer into any area where employees may be potentially exposed shall be reported in accordance with this subparagraph.

(i) A report of the occurrence of the incident and the facts obtainable at that time including a report on any medical treatment of affected employees shall be made within 24 hours to the appropriate OSHA Area Director.

(ii) A written report shall be filed with the appropriate OSHA Area Director within 15 calendar days thereafter and shall include:

(a) A specification of the amount of material released, the amount of time involved, and an explanation of the procedure used in determining this figure;

(b) A description of the area involved, and the extent of known and possible employee exposure and area contamination;

(c) A report of any medical treatment of affected employees, and any medical surveillance program implemented; and

(d) An analysis of the circumstances of the incident, and measures taken or to be taken, with specific completion dates, to avoid further similar releases.

h. ~~Medical Surveillance~~

(To be provided by NIOSH as soon as possible.)

OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION LETTER OF INTENT TO INITIATE D.C. PLAN REJECTION PROCESS, REASONS FOR NON-APPROVAL

Mr. Charles T. Greene
Director of Industrial Safety
Government of the District of Columbia
Minimum Wage and Industrial Safety Board
615 Eye Street, N.W.
Washington, D.C. 20001

Dear Mr. Greene:

I am enclosing a summary of the major areas in the District of Columbia Plan which would require modification in order to meet the requirements of section 18 of the Occupational Safety and Health Act of 1970 and the implementing regulations. Most, if not all, of these problems have been communicated to your staff on previous occasions and it is our understanding that you have

agreed to make numerous revisions in the plan. These include providing criminal penalties as stringent as those of the Federal program for willful violations causing death, unauthorized advance notice and false statements, making provision for formal establishment of abatement periods, and certain technical improvements.

However, we conclude that such revisions do not overcome the limitations of effectiveness resulting from enforcement of safety and health standards basically through criminal penalties. As explained more fully in the enclosed summary, these involve failure of such a system to provide for participation of employees as a matter of right in the review process and lack of the designated agency's control over interpretations of the law and its application in the review process.

CUSAROSS 00257

OSHA EMERGENCY TEMPORARY STANDARD ON VINYL CHLORIDE (TEXT)

Title 29—Labor

CHAPTER XVII—OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION, DE- PARTMENT OF LABOR

PART 1910—OCCUPATIONAL SAFETY AND HEALTH STANDARDS

Emergency Temporary Standard for Exposure to Vinyl Chloride

1. *Background.* Vinyl chloride (chloroethene), Chemical Abstracts Service Registry No. 75016, is a synthetic chemical made by oxychlorination of ethylene or by hydrochlorination of acetylene. It is the parent compound of a series of thermoplastic resin polymers and copolymers which are widely used for containers, wrapping tissues, electrical insulation, pipe, conduit and a variety of other products. Vinyl chloride has been made commercially in this country since 1939 and present production is in excess of seven billion pounds per year.

Vinyl chloride (VC) is a gas at ambient temperature and pressure and is a chlorinated hydrocarbon which has moderate liver toxicity. The present standard sets a ceiling value of 500 parts per million (ppm) (29 CFR 1910.93).

On January 22, 1974, the Occupational Safety and Health Administration was informed by the National Institute for Occupational Safety and Health (NIOSH) that the B. F. Goodrich Chemical Company reported that deaths of several of its employees from a rare form of liver cancer may have been occupationally related. As a result of this notification, and after consultation with NIOSH and a joint inspection of the plant by OSHA, NIOSH, and the Kentucky Department of Labor, a fact-finding hearing on possible hazards involved with the manufacture and use of both VC and polyvinyl chloride was announced on January 30, 1974 (39 FR 3874), and held on February 15, 1974.

2. *Carcinogenicity of VC.* Information produced at the hearing demonstrated that exposure of laboratory animals (mostly Sprague-Dawley rats) to VC by inhalation at and below the current OSHA standard of 500 ppm induced tumors, including angiosarcomas of the liver. Professor Cesare Maltoni, of the Instituto di Oncologia, Bologna, Italy, reported on a series of experiments on the effect of exposure of rats, mice, and hamsters to VC at concentrations of 10,000; 6,000; 2,500; 500; 250; and 50 ppm for varying periods of time (TR 43-63). Some of the experiments have been concluded, and others are still ongoing. The experimental results so far reported are that tumors have been observed in groups of animals exposed to VC at concentrations as low as 250 ppm. No tumors have been observed in the group of animals exposed to VC at a concentration of 50 ppm. It also appears so far that the total number of tumors, as well as the numbers of angiosarcomas of the liver, decrease as the concentrations of VC are reduced to 250 ppm. Finally, another experiment by Professor Maltoni is underway involving the exposure of 300 animals to VC at concentrations of

50 ppm, in order to assess in a more definitive way whether that level of exposure produces tumors in animals. Data reported by Torkelson, Oyen and Rowe (American Industrial Hygiene Association J 22:354-361 (1961)) indicate that exposure to VC at concentrations of 50 ppm failed to induce tumors in rats, hamsters, rabbits, and dogs.

The employees of the B. F. Goodrich Chemical Company who died from angiosarcoma of the liver had an average exposure of approximately 19 years to vinyl chloride, at unknown concentrations, and variable exposures to other volatile chemicals. (TR 93). Some employees of Union Carbide Company and Goodyear Company are also reported in a post-hearing comment from NIOSH dated March 11, 1974, to have had exposure to vinyl chloride and to have died from angiosarcoma of the liver. Finally, autopsies of four deceased employees revealed that liver angiosarcoma tumors were histologically indistinguishable from the angiosarcoma tumors observed in Professor Maltoni's experimental animals. It is concluded therefore, that vinyl chloride is carcinogenic for humans.

We therefore conclude that the present standard for VC should be lowered from a ceiling of 500 ppm to a ceiling of 50 ppm for the following reasons:

(a) In light of the evidence referred to above including the Maltoni experiments demonstrating that VC is carcinogenic in animals at 250 ppm, we conclude that VC must be considered carcinogenic in man at the same level;

(b) Although Professor Maltoni did not induce tumors in his experimental animals at an exposure concentration of 50 ppm, these data do not support the concept that occupational exposure of employees to concentrations of 50 ppm throughout their working lifetime would be without detrimental health effects;

(c) The question whether safe levels of exposure to carcinogens exist for humans and, if so, what such levels would be, is the subject of continuing scientific deliberation. In the case of VC, Professor Maltoni did not observe tumors in his animals at exposure concentrations of 50 ppm. In addition, Torkelson, Oyen, and Rowe found that exposure to concentrations of 50 ppm of VC failed to induce tumors in rats, hamsters, rabbits, and dogs. Accordingly, there is insufficient evidence at this time to conclude that VC at concentrations of 50 ppm or below poses a grave danger to humans.

(d) The emergency temporary standard adopted represents a substantial reduction in the permissible level of exposure and, in our practical judgment, is the lowest level that can be complied with immediately; and

(e) This standard will be in effect for a period of no longer than six months, during which time the whole question of possible safe exposure of humans to VC will be reconsidered more fully and in the light of more information, including experiments which are under way at this time (TR 47, 49, 71-74).

3. *Petitions for an emergency tempo-*

rary standard. In a telegram to the Assistant Secretary of Labor, received on or about March 14, 1974, the President of the United Rubber Workers International Union urged the establishment of an emergency temporary standard for VC. During the hearing of February 15, 1974, the Industrial Union Department, AFL-CIO, and the United Rubber Workers International Union made a joint petition for an emergency temporary standard for VC (TR 141-148), which was also joined by the Oil, Chemical and Atomic Workers International Union (TR 37). At the same hearing, several participants urged, on the other hand, a regular rulemaking proceeding as the most suitable for the orderly development of relevant information (TR 112, 180).

The petitions for an emergency temporary standard specified in detail the contents of the standard requested. In substance, the request is to issue a comprehensive fully-developed standard based on the recommendations of the Standards Advisory Committee on Carcinogens submitted to the Assistant Secretary of Labor on or about August 27, 1973. The recommendations are far-ranging, and cover special categories of operations, signs and labels, medical surveillance, reporting, etc., including a permit system for the use of a carcinogen.

We agree that an emergency temporary standard is necessary; we cannot say on the basis of the information developed so far that a comprehensive standard, such as the one requested, is either necessary or even desirable. It has been decided to promulgate a standard containing only those essential provisions which are deemed necessary to provide protection to employees from grave danger until a regular rulemaking proceeding in accordance with sections 6 (b) and (c) of the Act can be concluded. The reasons for a decision to establish a ceiling value of 50 ppm have already been stated. A decision on other possible, appropriate provisions is best made after consideration of all relevant data and views that interested persons may submit during the proceeding soon to be initiated.

With respect to arguments in opposition to issuance of an emergency temporary standard, the concern and efforts of several companies participating at the hearing for the protection of their employees are recognized. It may also be that some employers in some plants have fully complied with the interim controls recommended by NIOSH on January 30, 1974. There is, however, reason to believe that employees are currently being exposed to VC at concentrations well above 50 ppm. This was asserted several times at the hearing, and not seriously questioned. Moreover, a report, dated March 1974, of a survey by the staff of the Office of Standards Development, OSHA, of several facilities manufacturing VC and polyvinyl chloride revealed concentrations for some job classifications as high as 229 ppm. Therefore, a regulation is considered necessary to provide, immediately, adequate

posed to VC. Also, the eight-hour, time-weighted average standard suggested by several participants at the hearing (see, for instance, TR 178), has been rejected. The March 1974 report of the survey revealed that several kinds of work or operations are of short duration. Loading or unloading of a tank car may require approximately 15 minutes. The cleaning of a reactor may require approximately half an hour. An eight-hour, time-weighted average standard would permit exposure to VC at concentrations of 400 ppm for one hour. Such upward excursions, several times the 50 ppm level, cannot be permitted to occur.

4. *The standard.* The standard set out below contains only the requirements deemed necessary to provide protection before the conclusion of the rulemaking proceeding to be commenced shortly.

Because exposure to VC is hazardous, and because such exposure can occur in the processes of synthesizing or polymerizing of VC or in the handling of VC polymers or copolymers which contain absorbed VC, this standard applies to all such processes and to the handling, reacting, manufacturing, processing, re-leasing, repackaging, or storage of any of these materials. The monitoring requirements serve two purposes, to trigger into operation a compliance program and to check the effectiveness of the program. Also, engineering controls are favored for compliance, and respirators are intended to provide protection until such controls can be installed or in cases where such controls are not feasible.

Accordingly, by reason of the foregoing and on the basis of the record of the hearing of February 15, 1974, with exhibits, the written submissions received before the hearing pursuant to the notice of the hearing, the post-hearing written submissions by the participants at the hearing, the March 1974 report of a fact-finding survey recommendations received from NIOSH, and the other data referred to herein, it is found (1) that VC at concentrations in excess of 50 ppm is physically harmful and carcinogenic; (2) that exposure to VC at concentrations in excess of a concentration of 50 ppm poses a grave danger to employees; (3) that employees are presently exposed to VC at concentrations in excess of 50 ppm; and (4) that the emergency temporary standard set out below is necessary to provide immediate protection to employees from such danger.

Pursuant to section 6(e) of the Occupational Safety and Health Act of 1970, a proceeding will commence shortly in accordance with section 6(b) of the Act, in which the emergency temporary standard will serve as a proposed rule, together with other subsidiary rules. As soon as possible a draft environmental impact statement will be filed with the President's Council on Environmental Quality, and copies will be provided to other appropriate Federal agencies for their comments.

Pursuant to sections 6(c) and 8(c) (3) of the Williams-Steiger Occupational Safety and Health Act of 1970 (84 Stat. 1596, 1599; (29 U.S.C. 655, 657)), and

Secretary of Labor's Order No. 12-71 (36 FR 8754), 29 CFR Part 1910 is amended by adding thereto a new § 1910.93q to read as set forth below. In addition, pursuant to section 4(b) (2) of the Act (84 Stat. 1592; (29 U.S.C. 653)), the standard in the new § 1910.93q is determined to be more effective than the corresponding standards now in Subpart B of Part 1910, in Parts 1915, 1916, 1917, 1918, and 1926 of title 29, Code of Federal Regulations, and in Part 50-204 of Title 41 of the Code of Federal Regulations. Therefore, these corresponding standards are superseded by the new standard in § 1910.93q.

1. In 29 CFR Part 1910, § 1910.93 is amended by deleting from Table G-1 the line: " * * * C Vinyl chloride * * * 500 * * * 1300".

2. Part 1910 of Title 29 of the Code of Federal Regulations is amended by adding thereto a new § 1910.93q to read as follows:

§ 1910.93q Vinyl chloride.

(a) *Scope and application.* (1) This section applies to any area or operation in which vinyl chloride (chloroethene), Chemical Abstracts Service Registry Number 75015, is manufactured, reacted, handled, processed, released, repacked, or stored.

(2) This section does not apply to the handling, storage, or other use of vinyl chloride polymers and copolymers in the form of fabricated products.

(b) *Permissible exposure.* The occupational environment shall be controlled so that no employee is exposed to vinyl chloride at a concentration in excess of 50 parts per million (ppm) (127.0 mg/cum).

(c) *Monitoring.*—(1) *Initial monitoring.* As soon as possible but not later than April 22, 1974, every employer of an employee working in an area or operation in which vinyl chloride is manufactured, reacted, handled, processed, released, repacked, or stored shall begin monitoring the ambient air of the area to determine whether it contains vinyl chloride in concentrations in excess of 50 ppm.

(2) *Frequency.* Monitoring of a sufficient number of employees so that a representative sample of exposures to vinyl chloride may be determined shall be accomplished not less frequently than weekly until all results for three consecutive weeks are at or below 50 ppm. Thereafter, monitoring shall be conducted not less frequently than monthly so long as the concentrations of vinyl chloride do not exceed 50 ppm. If a monitoring sample reveals vinyl chloride in concentrations in excess of 50 ppm, weekly monitoring shall be resumed until all results for three consecutive weeks are at or below 50 ppm.

(3) *Method of monitoring.* Personnel monitoring shall be accomplished by collecting samples by suitable devices worn by the employee. The samples shall be analyzed by gas chromatography or by any other method which is of equivalent sensitivity. The analytical procedure shall be sensitive to 5 ppm of vinyl chloride in air with an accuracy of ± 20 percent for a ten minute air sample.

(4) *Employee observation of monitoring.* Employees working in an area or operation whose ambient air is monitored, or their representatives, shall be given a reasonable opportunity to observe the personnel monitoring required by this section.

(5) *Recordkeeping.* The results of all monitoring shall be recorded in writing. The records shall be retained for at least 5 years and shall be made available for inspection and copying by representatives of the Assistant Secretary of Labor for Occupational Safety and Health and the Director of the National Institute for Occupational Safety and Health (NIOSH).

(6) *Employee access.* Each employee and former employee shall have access to such records of the results of monitoring required by this section as will indicate his own exposure to airborne concentrations of vinyl chloride.

(7) *Employee notification.* Each employer shall promptly notify any employee who has been or is being exposed to vinyl chloride in concentrations in excess of 50 ppm, and shall inform him of the corrective action being taken.

(d) *Compliance.* (1) Whenever any monitoring sample reveals vinyl chloride at a concentration in excess of 50 ppm, or whenever any accident, such as rupture of equipment or spillage, indicates the likelihood of a greater than usual release of vinyl chloride into the ambient air, all employees exposed to such concentrations shall be withdrawn to a safe area and shall not be permitted to re-enter the work area unless they wear either Type C continuous flow or pressure demand air supplied respirators or self-contained breathing apparatus.

(2) Work which may reasonably be expected to release vinyl chloride in concentrations in excess of 50 ppm, such as repair, maintenance or cleaning of reactors or other equipment containing vinyl chloride, shall be accomplished only by employees wearing Type C continuous flow or pressure demand air supplied respirators or self-contained breathing apparatus.

(3) In any case covered by paragraphs (d) (1) or (d) (2) of this section, in addition to providing the required respirators, the employer shall examine and analyze the source of the excessive concentrations of vinyl chloride in order to determine feasible engineering or operational controls appropriate to reduce the airborne concentrations to the permissible level. Such controls shall be implemented as quickly as possible.

(4) Periodic tests shall be conducted for equipment leaks and for emissions of vinyl chloride which may result from work practices.

3. In 29 CFR Part 1910, § 1910.19 is revised to read as follows:

§ 1910.19 Special provisions for air contaminants.

(a) *Asbestos dust.* Section 1910.93a shall apply to the exposure of every employee to asbestos dust in every employment and place of employment covered by § 1910.12, § 1910.13, § 1910.14, § 1910.15, or § 1910.16, in lieu of any dif-

ferent standard on exposure to asbestos dust which would otherwise be applicable by virtue of any of those sections.

(b) *Vinyl chloride*. Section 1910.93q shall apply to the exposure of every employee to vinyl chloride in every employment and place of employment covered by § 1910.12, § 1910.13, § 1910.14, § 1910.15, or § 1910.16, in lieu of any dif-

ferent standard on exposure to vinyl chloride which would otherwise be applicable by virtue of any of those sections.

Effective date. These amendments shall become effective on April 5, 1974. (Secs. 4, 6, and 8, 84 Stat. 1592, 1596, 1599 (29

U.S.C. 653, 655, 657); Secretary of Labor's Order No. 12-71, 36 FR 6754.)

Signed at Washington, DC., this 2d day of April 1974.

JOHN STENDER,
Assistant Secretary of Labor.
[FR Doc. 74-7890 Filed 4-4-74; 8:45 am]

-- End of Text --

-- End of Section E --

CUSAROSS 00260

IMA REPORT

April, 1974

NATIONWIDE SURVEILLANCE OF ANGIOSARCOMA OF THE LIVER IN U.S.

Physicians who have patients under their care with a diagnosis of angiosarcoma of the liver, or who have encountered such cases in their practice over the past 10 years, are urged to contact the U.S. Center for Disease Control in Atlanta. Information concerning all such cases, regardless of assumed etiology, should be mailed to Center for Disease Control, Bldg. 1, Room 520, Atlanta, Ga. 30333, or telephoned to (404) 633-3311, ext. 3961.

Such information will become a part of a national surveillance registry for cases of angiosarcoma of the liver in the United States which was recently established by the National Institute for Occupational Safety and Health and the Disease Center's Bureau of Epidemiology in response to the recent discovery of the possible relationship of this exceedingly rare tumor to vinyl chloride exposure. Since January of this year when The B.F. Goodrich Chemical Company reported the first suspicions that vinyl chloride might be implicated in four cases of angiosarcoma of the liver that occurred among employees who had spent many years in vinyl chloride operations, three additional cases have been identified in workers at this plant, and single cases have been reported at two other plants.

✓ All four of the initial patients had worked in various phases of the vinyl chloride polymerization process for at least 14 years before diagnosis, and each showed evidence of coexisting hepatic fibrosis in the absence of heavy alcohol intake, prior hepatitis, or exposure to hepatotoxic agents outside the work environment. In particular, there was no evidence of exposure to thorium dioxide or arsenic, two chemicals previously implicated as causes of this tumor in man. Epidemiologic studies are underway to define more precisely this apparent relationship between hepatic angiosarcoma and exposure to vinyl chloride. The national surveillance registry is a vital part of this effort, both as a measure of past and present incidence in the United States, and as a means by which to gauge what proportion of cases may indeed be related to vinyl chloride. Full participation by physicians in this surveillance effort is urgently solicited by Marcus Key, M.D., NIOSH Director, and Clark W. Heath, Jr., M.D., Chief of the Cancer and Birth Defects Division of the Bureau of Epidemiology.

Health Hazards

EASTMAN KODAK SUBSIDIARY ISSUES PRELIMINARY REPORT ON MBK EXPOSURE

Exposure of rats and guinea pigs to high concentrations of methyl butyl ketone (MBK) through inhalation and dermal contact produced serious health effects, a preliminary study by Eastman Chemical Products, Inc., indicated.

As a result of the study, which was forwarded voluntarily by Eastman Chemicals to the National Institute for Occupational Safety and Health, and to its 2,000 customers, some action by NIOSH can be expected within the next two weeks, OSHR was told. Exposure of workers to MBK has been used to link peripheral neuropathy and polyneuritis suffered by workers at Columbus Coated Fabrics, Inc., which has formed the basis of an extensive dispute between labor and management at the firm's Columbus, Ohio, plant (Current Report, March 7, p. 1251).

The studies involved exposure of concentrations of MBK, methyl ethyl ketone (MEK), and methyl isobutyl ketone (MIBK) to dogs, monkeys, and rats. Inhalation rates ranged from 1,300 to 2,000 ppm for six hours a day, five days a week during a four-month period, OSHR was told. Although results on the dogs and monkeys were inconclusive, all six rats in the tests showed changes in the nerves characteristic of peripheral neuropathy. The rats underwent 61 exposures at levels many times higher than the occupational level of 100 ppm. In addition the rats all had signs of hind leg footdrop, the study found.

Exposure of the animals to MEK and MIBK did not produce conclusive results, according to the study.

Dermal Exposure

Guinea pigs were treated with skin applications of MBK during a four-month period. For the first four weeks 802 mig were applied to the animals once a day, while for the final 14 weeks, they were given 1604 mig twice a day. At the end of the study the animals were found to have a blood concentration of MBK equal to 10 percent of the original application.

Eastman Chemicals issued a letter on March 1 to its 2,000 customers outlining the results of the study and recommending procedures to be followed until upper levels of occupational exposure to MBK can be established. Among the recommendations were the following steps:

- Contact of the skin and eyes with MBK should be avoided by use of protective clothing and protective eye equipment.
- In conditions where spills of MBK are possible, respiratory equipment for personnel who might be exposed should be utilized.
- Where there is contact between MBK and the skin, the skin should be washed immediately with water.
- Exhaust ventilation should be used to keep exposure levels to MBK below 100 ppm.

HEALTH HAZARD EVALUATION DETERMINATION

REPORT 72-58

CITY FOODS
SEATTLE, WASHINGTON

SEPTEMBER 1973

I. TOXICITY DETERMINATION

In response to six requests for Health Hazard Evaluations from retail meat wrapping employees in and around Seattle, Washington, regarding exposure to the thermal decomposition products of polyvinyl chloride (PVC) meat packaging film, a limited study of retail meat wrappers was undertaken. Although the data presented in this report did not result from direct evaluation of the work environment at the City Foods, Seattle, Washington, the findings of this study are generally applicable to retail meat wrapping operations using PVC meat packaging films.

It has been determined that air contaminants generated by the thermal cutting of polyvinyl chloride (PVC) packaging films in conjunction with the wrapping of meat are potentially toxic to some meat wrapping employees. This determination is based upon medical evidence compiled during a limited study of meat wrappers in the United States. This study involved a review of the pertinent scientific literature, consultation with researchers in this area of investigation, the collection of medical histories, clinical observations at the worksite, pulmonary function testing of meat wrappers, and consideration of wrapping procedures, equipment, and meat wrapping environmental conditions.

Evidence suggests that a sizeable percentage of meat wrappers suffer from mild symptoms to include eye, nose, and throat irritation. A portion of these affected meat wrappers who have an underlying predisposition to respiratory difficulties resulting from a variety of conditions (tobacco abuse, asthma, emphysema, and other serious respiratory diseases) experience more serious respiratory problems. These can include shortness of breath, difficulty in breathing, coughing, and general physical distress. This study has not established whether or not presently healthy meat wrappers may develop respiratory difficulties after prolonged exposures to contaminants from thermal decomposition of PVC packaging films.

Although substances in the meat wrapping environment other than those associated with PVC films may be responsible for the previously stated clinical manifestations, the available evidence strongly implies that the air contamination from thermal cutting of PVC packaging film is the causative agent. As yet, the patho-physiologic mechanism for this malady is not clearly understood.

Based on present experience with this particular problem, it is recommended that the following practices be instituted:

1. Pre-employment physical examinations, including chest x-rays and pulmonary function tests be performed on all individuals entering the meat wrapping industry. (Individuals who are found to have severely compromised pulmonary function or who exhibit strong predisposition to pulmonary disorders should not enter the meat wrapping profession.)
2. Meat wrapping machinery should be clean and well maintained. Machines with controlled low temperature cut-off wires are to be preferred. (There is need for further study with regard to controlling contamination at its source via new cutting mechanisms or local exhaust ventilation, etc.)
3. Meat wrapping should be conducted in well ventilated surroundings.

II. DISTRIBUTION AND AVAILABILITY OF THE DETERMINATION REPORT

Copies of this Determination Report are available upon request from the Hazard Evaluation Services Branch, NIOSH, U.S. Post Office Building, Room 508, 5th and Walnut Streets, Cincinnati, Ohio 45202. Copies have been sent to:

- a) City Foods, Seattle, Washington
- b) Authorized representative of employees
- c) U. S. Department of Labor - Region X
- d) NIOSH - Region X
- e) Washington State Department of Labor and Industries

For the purposes of informing the 1-3 affected meat wrappers the employer will promptly "post" the Determination Report in a prominent places near where affected employees work for a period of 30 calendar days.

III. INTRODUCTION

Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669 (a)(6), authorizes the Secretary of Health, Education, and Welfare, following written request by any employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The National Institute for Occupational Safety and Health (NIOSH) received such a request from an authorized representative of the meat wrapping employees at the City Foods, Seattle, Washington,

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as well as from five other stores in Seattle, Washington area regarding employee exposures to the potentially toxic substances emitted from thermal decomposition of polyvinyl (PVC) packaging films in use in the meat department. One to three meat wrapping employees are employed in each of these stores and are subsequently exposed to the substances in question.

IV. HEALTH HAZARD EVALUATION

A. Description of Process - Conditions of Use

Although several types of meat wrapping machines were observed during the course of this study, most machines incorporated the basic features of the "typical" hand wrapping machine shown in Figure 1.

Wrapping meat involves: (1) pulling out a desired length of film, (2) wrapping the film around a tray or cut of meat, (3) severing the film from the supply roll using the hot wire cut-off, (4) folding the film ends under the package, and (5) sealing the folded ends under the package by touching the package to the heated pad.

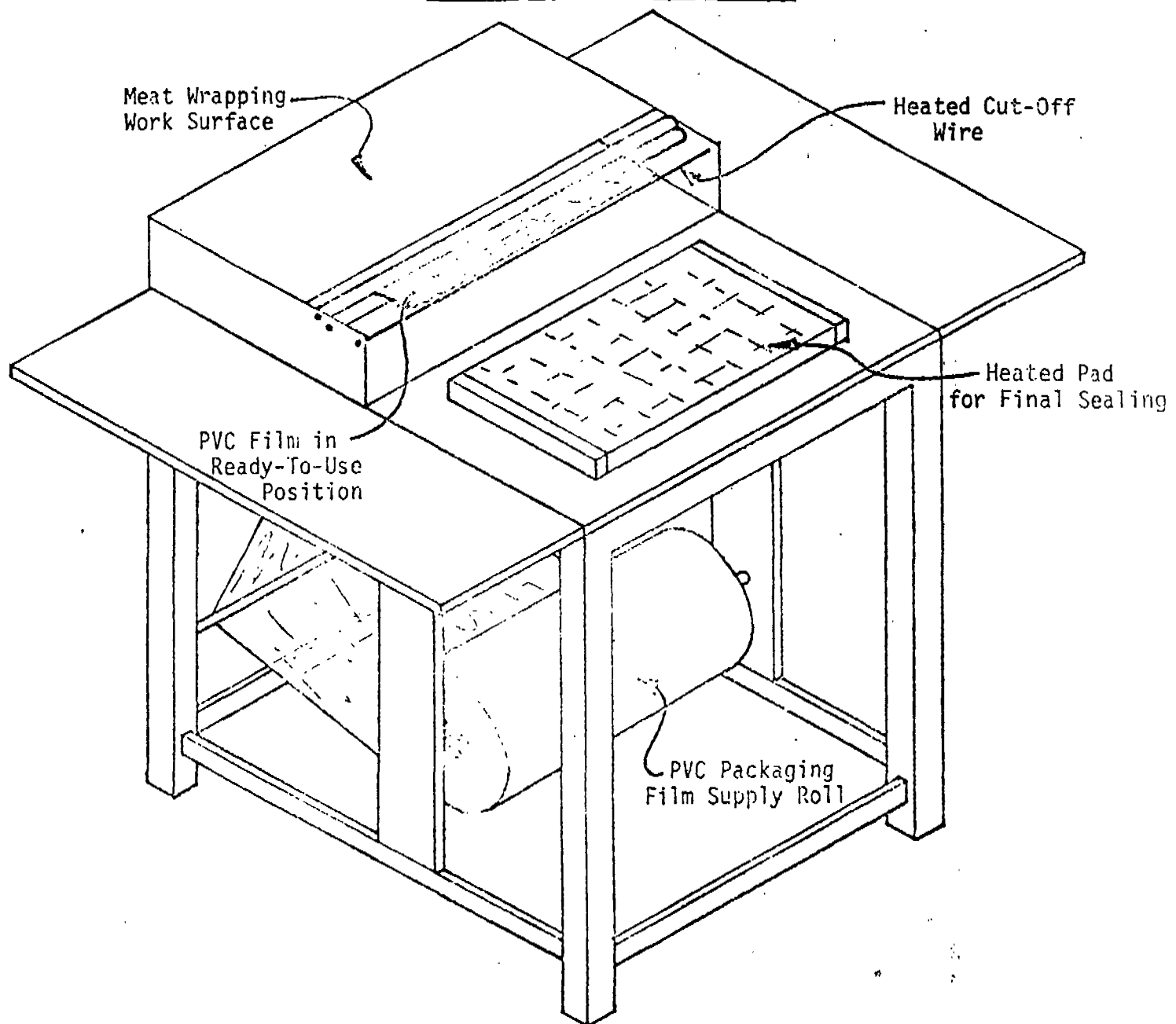
Air contaminants generated by the hot wire cutting of PVC packaging films and their alleged toxic effects on meat wrapping employees constitute the subject of this health hazard evaluation. There are approximately 75,000 meat wrapping employees in the United States, according to union and industry estimates.

B. Study Background and Design

Polyvinyl chloride and wrapping film is made from pure PVC resin and a variety of additives. All additives must be approved by the federal Food and Drug Administration for use in meat packaging materials. These additives include plasticizers, stabilizers, antifog agents, lubricants, and colorants. Plasticizers (dioctyl adipate - di-2-ethyl hexyl adipate, and epoxidized soya or soybean oil) can comprise up to 30% of the film. Stabilizers (calcium-zinc stearate) antifog agents (e.g., polyoxyethylene derivatives of sorbitan monooleate), lubricants (e.g., stearic acid), and colorants together makeup roughly 2-6% of the film.

Several investigators have attempted to identify and quantitate air contaminants generated by the hot wire cutting of PVC film in the meat wrapping environment. Early field measurements for hydrogen chloride (HCl) detected trace amounts (less than 1 ppm) in the vicinity of meat wrapping operations.² A later laboratory study of air contaminants from hot wire cutting of PVC film confirmed the presence of HCl and related its rate of generation together with the rate of generation of particulate to the operating temperature of the hot wire.³ As would be expected, the production of both HCl and airborne particulate increase with increasing wire temperature.

FIGURE 1: Typical Hand-Wrapping Machine



Manufacturers of Wrapping Equipment: Automatic, Semi-Automatic, and Hand Wrapping

Cleveland-Detroit Corporation, Clamco Division
J. B. Dove and Sons, Incorporated
Heat Sealing Equipment Manufacturing Company
The Hobart Manufacturing Company
Package Machinery Company
Reliance Electric Company, Toledo Scales and Systems

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To date, three researchers have found the film plasticizer to be the predominant contaminant generated by the thermal decomposition of PVC meat wrapping film.³⁻⁵ The oral toxicity of di-2-ethyl hexyl adipate, as determined by animal experimentation, is relatively low. However, no data are currently available regarding the inhalation toxicity of di-2-ethyl hexyl adipate. It is interesting to note that one researcher, Bovee, et al. identified the plasticizer to be diisooctyl adipate while the other two (Van Houten and Jaeger) found di-2-ethyl hexyl adipate. Diisooctyl adipate has exactly the same molecular weight as di-2-ethyl hexyl adipate and possesses very similar physical properties.

Hydrogen chloride is possibly the second most important degradation product. HCl can be detected at concentrations of 1-5 ppm and is disagreeable at concentrations of 5-10 ppm.

Other film degradation products have been identified, but are present in small quantities when compared to the film plasticizer. These other materials include chlorinated hydrocarbons and breakdown products of film additives.

Workplace concentrations of PVC film decomposition products are difficult to measure. As previously, stated, HCl has been found in very low concentrations in the meat wrapping environment. Laboratory experiments by Van Houten et al. suggest that airborne concentrations of HCl in the plume of "smoke" directly over the hot wire can reach 2 ppm. These measurements were made during "artificially severe operating conditions," which would rarely occur during actual meat wrapping. (It should also be noted that an employee's exposure would be to a significantly lower concentration than that found in the plume close to the wire. In the same study plasticizer concentrations in the plume were found as high as 13 mg/M³. Again, this value was found during artificially severe operating conditions.

Clinical complaints allegedly resulting from exposure to air contaminants from PVC meat wrapping film were first referenced in an unpublished study conducted by NIOSH's predecessor the Bureau of Occupational Safety and Health.² According to that investigation, state health officials in Virginia became involved with complaints from meat wrappers in the summer of 1969. Since that time complaints have come in by letter and telephone from several cities across the Nation. Due to the informal nature of most of the reports, it is difficult to accurately estimate the true number of individuals involved. However, a small group of medical investigators scattered throughout the Nation have reported approximately 50-75 cases of pronounced clinical symptoms.

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Subjective estimates from union officials, university investigators, medical professionals, and meat wrappers suggest that a large number of meat wrappers are less seriously affected.

To better delineate the clinical manifestations of exposure to contaminants from PVC film decomposition a preliminary survey of meat wrapping operations was made. Five retail stores in and around Seattle, Washington were visited during August 7-9, 1972. Meat wrapping operations were observed in each retail store and eighteen meat wrappers with varied work experience with PVC films were interviewed. Each worker was questioned in an attempt to elicit symptoms of upper respiratory tract irritation, irritation of the eyes, nose, and throat, and occupational dermatoses. Spirometric measurements were obtained from thirteen of the meat wrappers.

At the completion of this preliminary survey it was clear that a more detailed scientific study would be necessary to elucidate the full ramifications of the potential health problems associated with the use of PVC films. The assistance of the Amalgamated Meat Cutters and Butcher Workmen of North America was solicited to facilitate the location of metropolitan areas where sizeable numbers of meat wrappers were allegedly being adversely affected by air contaminants from PVC films. Following a nationwide search, the City of Louisville, Kentucky was selected as a site for further investigatory research.

A research protocol was developed under the guidance of pulmonary specialists from the NIOSH Appalachian Laboratory of Occupational Respiratory Diseases. The protocol called for the administration of a health questionnaire and the conduction of pulmonary function testing on meat wrappers and suitable controls. The orientation of the questionnaire and the subsequent interview with a NIOSH physician placed emphasis on occupationally related health problems, especially respiratory health problems.

On January 22, 1973, in Louisville, Kentucky, seventeen meat wrappers and twenty non-meat wrappers (office personnel serving as controls) completed medical questionnaires and participated in pre- and post-workshift pulmonary function testing. Technical problems regarding environmental sampling prevented evaluation of employee exposures on the day of testing. As observed in a number of retail establishments, meat wrappers' exposures to contaminants from hot wire cutting of PVC meat packaging film are intermittent and highly variable. To be useful in interpreting employee symptoms, breathing zone air samples would have to reflect both average and short term exposures. Although these contaminants have been measured in undiluted form near the source of generation³, there is at present no suitable method of sufficient sensitivity to measure variable breathing zone concentrations.

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C. Evaluation Methods

1. Medical Questionnaire

The medical questionnaire consisted of twenty-six sets of questions. Its purpose as to gather pertinent information concerning an individual's past medical history, smoking history, past occupational exposures, current respiratory status and adverse effects allegedly arising from exposure to air contaminants from PVC films.

2. Pulmonary Function Testing

Each pulmonary function test required the employee to make three forced expiratory volume practice maneuvers after which three forced expiratory volume maneuvers (reproducible within 5%) were recorded as flow volume loops. A waterless, high fidelity spirometer equipped with an air temperature probe was used. The flow volume loops were displayed on a storage oscilloscope and recorded on magnetic tape. A photograph of each oscilloscope display was taken for backup. Computer analysis of flow volume loops provided the following parameters forced expiratory volume in one second (FEV₁), and flow rates at 25, 50, 75 and 90 per cent of forced vital capacity (FVC).

D. Evaluation Results

1. Preliminary Survey (Seattle, Washington and vicinity)

Sixteen of the eighteen meat wrappers interviewed in the preliminary survey were known to have suffered ill effects from air contaminants from PVC films. Only two workers were free of any clinical symptomatology. Eight had similar case histories and admitted experiencing varying degrees of sneezing, rhinorrhea, and eye irritation. Most individuals gave a like story that the ill effects came on from one to three hours after the commencement of meat wrapping in the morning. The workers stated that as the workday progressed the prodromal manifestations increased in intensity. The sneezing, rhinorrhea, and throat and eye irritation would abate in the evening hours and would be non-existent during week-ends and vacations.

Five workers experienced more severe clinical symptomatology necessitating physician intervention and, on occasion, hospitalization. These individuals seemed to suffer with "occupational bronchiolitis." They suffered at times with severe dyspnea, productive cough, and nasal congestion. Onset of these symptoms was from one-half to two and one-half hours after commencement of work. These ill effects led to increased absenteeism. All were on one form of medication or another. This group also stated that a period of several days away from the meat wrapping environment was required for them to feel like their normal selves.

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Four of these workers had fifteen or more pack-years of cigarette smoking behind them.

Three meat wrappers had pre-existing susceptibility to upper respiratory symptomatology caused by severe disease processes (rheumatic fever, chronic obstructive pulmonary disease, and lung abscess).

2. Medical Questionnaires (Louisville Study)

Seventeen meat wrappers and a control population of twenty individuals completed the questionnaire. None of the controls reported any adverse clinical symptomatology associated with their particular form of employment. The majority of the controls worked as clerks in retail grocery stores.

As a group the seventeen meat wrappers averaged nine years and three months of experience in the meat wrapping profession. Forty-five per cent of these meat wrappers complained of irritation from film contaminants which resulted in watering and itching eyes. Thirty per cent of the wrappers complained of burning or dryness of the throat. Three wrappers (18%) stated that they experienced "painful breathing" and shortness of breath while working with PVC meat wrap. It is important to note that these same three individuals had a history of allergies, were on medication and were under physician care.

3. Pulmonary Function Testing (Louisville Study)

All pulmonary function data were analyzed by bio-statisticians at the NIOSH Appalachian Laboratory for Respiratory Diseases. The data can be summarized by examining the following statistical tests:

Note: df = degrees of freedom (number of employees tested minus one)

P = probability that a difference occurred by chance alone.

The "student t test" was used to determine whether there were significant differences between groups of individuals with respect to changes in FEV_1 's and FVC's. To be significant, a difference between groups would have a probability of occurring by chance of less than 5% or P less than 0.05.

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Test No. 1 - When all exposed (meat wrappers) were compared with all non-exposed (controls) with respect to any differences between pre- and post-workshift values of FEV₁ and FVC, there was no significant difference at the 95% confidence level (i.e. P less than 0.05).

$$\begin{array}{ll} T_{FEV_1} (35df) = -0.35 & P = 0.73 \\ T_{FVC} (35df) = -0.42 & P = 0.67 \end{array}$$

Test No. 2 - When exposed smokers were compared with non-exposed smokers, there was no significant difference.

$$\begin{array}{ll} T_{FEV_1} (11df) = 0.22 & P = 0.83 \\ T_{FVC} (11df) = 0.31 & P = 0.76 \end{array}$$

Test No. 3 - When exposed non-smokers were compared with non-exposed non-smokers there was no significant difference.

$$\begin{array}{ll} T_{FEV_1} (22df) = 0.55 & P = 0.59 \\ T_{FVC} (22df) = 0.11 & P = 0.90 \end{array}$$

Test No. 4 - Test No. 1 was repeated with respect to peak flow and flow at 25, 50, 75 and 90% of FVC. There was a significant difference for F90.

$$\begin{array}{ll} T_{PF} (35df) = 0.47 & P = 0.64 \\ T_{F25} (35df) = 0.38 & P = 0.71 \\ T_{F50} (35df) = 0.01 & P = 0.99 \\ T_{F75} (35df) = 0.11 & P = 0.91 \\ T_{F90} (35df) = 2.39 & P = 0.02 \end{array}$$

Test No. 5 - Test No. 2 was repeated with respect to the preceding parameters and there was a significant difference for F50.

$$\begin{array}{ll} T_{PF} (11df) = 0.08 & P = 0.94 \\ T_{F25} (11df) = 1.36 & P = 0.20 \\ T_{F50} (11df) = 2.31 & P = 0.04 \\ T_{F75} (11df) = 0.88 & P = 0.40 \\ T_{F90} (11df) = 0.54 & P = 0.60 \end{array}$$

Test No. 6 - Test No. 3 was repeated with respect to the preceding parameters and there were significant differences for F75 and F90.

$$\begin{array}{ll} T_{PF} (22df) = 1.14 & P = 0.27 \\ T_{F25} (22df) = 0.98 & P = 0.34 \\ T_{F50} (22df) = 1.61 & P = 0.12 \\ T_{F75} (22df) = 2.26 & P = 0.03 \\ T_{F90} (22df) = 2.87 & P = 0.01 \end{array}$$

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In summary, pulmonary function tests of this small, randomly selected population of meat wrappers revealed no gross pulmonary effects in comparison to a control population after one workshift of meat wrapping. Furthermore, it must be stated that this exposed study group was of general good health and free of serious symptomatology.

E. Discussion

A study of meat wrapping employees is beset by various intrinsic problems from the onset. These include the following:

- a) Low density dispersal of meat wrappers in any geographic area.
- b) No more than two or three meat wrappers employed at any typical retail store.
- c) Meat wrapping work environments, although similar, are not strictly uniform. Differences can exist in packaging equipment (i.e., operating parameters), type of wrapping material ambient environmental conditions (temperature, humidity), general ventilation provisions, work practices, and volume of meat wrapping performed.
- d) Work shifts for meat wrapping employees are highly variable.
- e) There is a lack of suitable sampling and analytical methodology for the evaluation of employee exposures to PVC film decomposition products encountered in retail meat wrapping. At present, methods are not sensitive enough to characterize intermittent exposures or variable constant exposure via breathing zone sampling techniques.

The above problems interrupted the completion of this preliminary controlled scientific study. At this point, a limited amount of data have been compiled for a population of basically healthy meat wrappers. There remains the necessity to study a sizeable population of seriously affected meat wrappers. It is felt that such a population exists based upon scattered reports of clinical symptomatology from various medical investigators throughout the Nation.

V. REFERENCES

- 1. Vandervort, Robert - Personal Communication by Letter with Major Film Manufacturers, 1970.
- 2. Vandervort, R. "Polyvinyl Chloride Meat Wrapping Film Study," unpublished USPHS, BOSH, DOIDC, Technical Assistance Report, Cincinnati, Ohio (1971).

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3. Van Houten, R., A. L. Cudworth, C.H. Irvine. Evaluation and Reduction of Air Contaminants Produced by Thermo Cutting and Sealing of PVC Packaging Film. Liberty Mutual Insurance Company, Hopkinton, Mass. (Unpublished).
4. Bovee, H.H., L.E. Monteith, and R.M. Orheim. Thermal Decomposition of Meat Wrapping Film. Department of Environmental Health, School of Public Health and Community Medicine, University of Washington. (Unpublished).
5. Vandervort, Robert - Personal Communication by telephone with Dr. Rudolph Jaeger, Associate Professor of Toxicology at Harvard University School of Public Health.
6. Patty, F.A. Industrial Hygiene and Toxicology, Vol. II, John Wiley & Sons, 1963.

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Occupational Acroosteolysis

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and Marvin S. Kerzner, MD, Providence, RI

Occupational acroosteolysis is an unusual disease in which affected persons have sclerodermoid-like lesions of the skin, conditions similar to Raynaud's phenomenon, and asymptomatic, bony defects of the extremities. To our knowledge, the disease is confined solely to workers in the plastics industry, specifically those engaged in the production of polyvinyl chloride from vinyl chloride. The incidence of the disease is unknown but is thought to occur in 3% or less of workers.

It is indeed impressive to note that although the industrial process of polymerization of polyvinyl chloride (a solid plastic material) from vinyl chloride (a gas) has been widely used in the plastics industry throughout the world for three decades or more, the disease, occupational acroosteolysis, which is apparently related to this process, did not emerge as a new clinical entity until 1963.¹

It is even more impressive to us as dermatologists to note that although the initial complaints or manifestations of the disease and most of the debility related to it are of a dermatologic nature, ie, "Raynaud's-like phenomenon," and increased thickening and tightness of the hands, there is little information regarding this disease in the dermatological literature. Therefore, we wish to report two cases of this unique disease and to review the present state of our knowledge regarding the incidence, cause, sequel, treatment, and prognosis.

Report of Cases

CASE 1.—A 27-year-old white man entered the Roger Williams General Hospital for evaluation of tightness of the hands and wrists of approximately four months' duration. Two years prior to admission to the hospital, the patient worked in the manufacture of polyvinyl chloride as a vat cleaner for six months and thereafter as a bagger. One year prior to admission, the patient first began to note blanching of his hands upon exposure to cold that in time progressed into a bluish cyanosis of the hands accompanied by severe pain.

He was seen by a local physician and was given indomethacin after being told that he had gout. Eight months later, the patient began to notice progressive thickening of his hands and forearms with limitation of motion of the digits of both hands and the shoulder girdle, and sporadic arthralgia. Two weeks prior to hospitalization, he accompanied his mother on her routine visit to her physician who noted the obvious changes in the skin of his hands and wrists, and recommended hospitalization.

Pertinent physical findings were limited to the integument. The hands were diffusely pink in color, and on extension or flexion of the digits became totally blanched. The examiner was unable to move the skin over the underlying subcutaneous structure. There was a continuation of the skin involvement from the hands to the forearms and elbows with an accentuation and tendency for nodule or plaque formation about the extensor and flexor tendons of the hands and at the wrists (Fig 1 and 2). It was very striking to note that in the presence of the sclerodermatous appearance of the affected parts, there was minimal or no loss of hair. The patient was unable to tightly clench the fists. The lower extremities were normal except for the feet which had a mottled cyanotic appearance and thickened cords of skin on the dorsum of the right foot. The facial skin did not reveal stiffening beneath the eyelids or perioral radial furrowing. Telangiectasia was absent on the affected parts, fingernails, central portion of the face, and intraorally.

The following laboratory tests were performed, disclosing values which are within normal limits: hemoglobin, 14.7 gm/100 ml; hematocrit reading, 45%; white blood cell count, 9,500/cu mm; differential cell count: 70% segmented neutrophils, 28% lymphocytes, 2% monocytes; serum calcium, 9.9 mg/100 ml; phosphorus, 4.7 mg/100 ml; blood glucose, 101 mg/100 ml; blood urea nitrogen, 16 mg/100 ml; uric acid, 7.2 mg/100 ml; cholesterol, 253 mg/100 ml; total protein, 7.6 gm/100 ml; albumin, 4.9 gm/100 ml; total bilirubin, 0.2 mg/100 ml; alkaline phosphatase, 40 units/100 ml; lactic dehydrogenase, 125 units/ml; serum glutamic oxaloacetic transaminase, 37 units; creatinine, 1.1 mg/100 ml; sodium, 141 mEq/liter; chloride, 101 mEq/liter; potassium, 4.4 mEq/liter; venous pH, 7.36; arterial carbon dioxide pressure, 48 vol%; total carbon dioxide, 27.5 mEq/liter. The following tests were negative or within normal limits: latex fixation for rheumatoid arthritis, C-reactive protein, antinuclear antibodies, VDRL test for syphilis, LE preparation (three times), creatinine clearance, thiodothyronine uptake (28%), urinalysis, and immunoelectrophoresis of serum. Results of pulmonary function studies were within normal limits. An x-ray film of the chest was normal.

X-ray films of the hands (Feb 26, 1970) revealed a fracture of the tip of the distal phalanx of the left middle finger (Fig 3). The results of additional studies of the forearms, elbows, arms, shoulders, and chest were within normal limits. The results of esophageal motility studies and roentgenograms of the upper gastrointestinal tract were found to be normal, and an incidental finding of osteitis condensans ilii was noted.

Follow-up x-ray films on Feb 16, 1971, revealed further bony loss and resorption of several distal phalanges of the right hand with the first, second, and fourth being most severely involved. The left hand had similarly undergone further resorptive changes with the first, second, and third distal phalanges being most severely involved (Fig 4).

Hematoxylin and eosin-stained sections of the skin of the forearm demonstrated a normal epidermis and skin appendages that were normal in size and distribution

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Fig 1.—Cutaneous findings observed in occupational acroosteolysis. Note erythema, blanching, and thickening of digits, and ropy appearance of skin on dorsal surfaces (case 1).

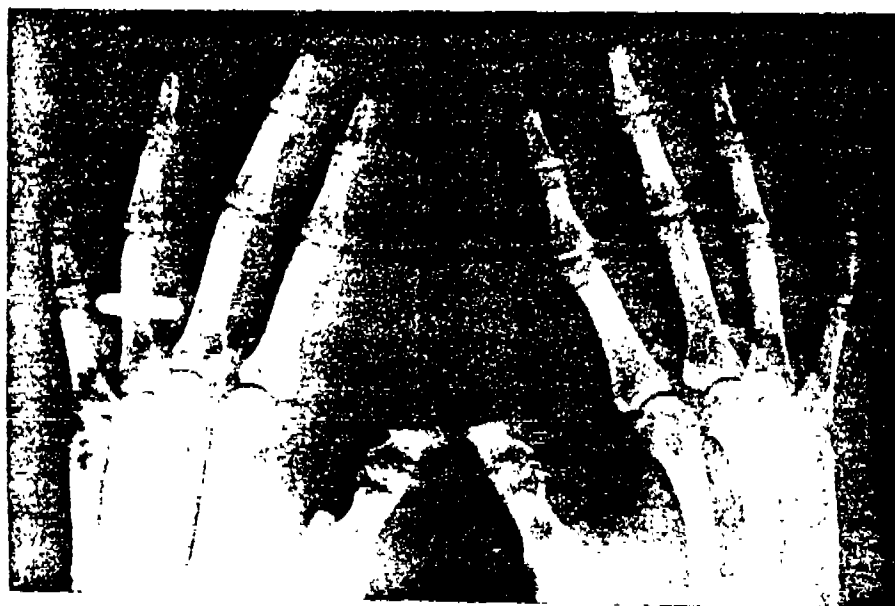


Fig 2.—Forearm shows thickened, lobular or ropy nature of skin in occupational acroosteolysis. Hair appears normal in texture and distribution (case 1).



Fig 3.—X-ray film of both hands taken Feb 26, 1970. Note lytic lesion at tip of distal phalanx on digit 3, left hand. Right hand appears normal (case 1).

Fig 4.—X-ray film of both hands taken Aug 24, 1971. Note increase in number of lytic lesions in distal phalanges of both hands, and more severe bony destruction in left hand (case 1).



(Fig 5). Pathological changes were most pronounced in the dermis, which appeared considerably thickened. The dermal changes were characterized by a nonfibrillary homogenization of the collagen and by the presence of thickened swollen collagen bundles radiating in all directions. These thickened bundles of collagen showed accentuated staining properties with eosin. There was some degree of interstitial edema, and an inflammatory infiltrate with a predominantly perivascular distribution made of lymphocytes, and a few histiocytes, were also seen (Fig 6). These changes of the collagen were noted throughout the dermis and around the sweat glands. There was no subcutaneous fat observed. Verhoeff's elastica stain showed disorganization of the elastic fibers, which appeared to be split and broken in some areas and condensed into thick bundles in other areas (Fig 7). Jancso's chlorazol fast pink and Congo-red fast green stains were done to detect the presence of particulate material which could have been identified as vinyl compound. These were negative. Toluidine blue and Alcian blue stains revealed metachromatic staining material within the interstices of the thickened collagen bundles. When the specimen was studied under polarized light, two types of collagen bundles were noted: a small number of large, thick bundles which polarized bright yellow, and a larger number of smaller bundles which did not polarize at all (Fig 8).

CASE 2.—The patient is a 29-year-old white man with a history of employment in the vinyl chloride polymerization industry for the past four years. He worked as a vat operator and reactor cleaner for 12 months and subsequently as a chemical operator.

In June 1970, the patient noticed a full



Fig 5.—Hematoxylin and eosin-stained section of involved skin showing normal epidermis and normal location of sweat ducts. Note swollen and thickened collagen (x40).

Fig 6.—Thickened bundles of collagen with accentuated eosinophilic staining properties. Note prominence of interstitial edema (x250).

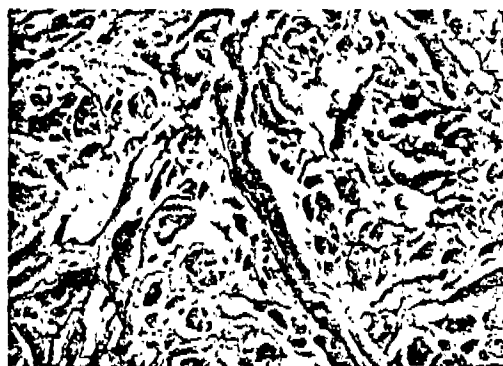


Fig 7.—Verhoeff's-stained section showing disorganization of elastic fibers, some fragmented, others condensed into thick bundles (x250).

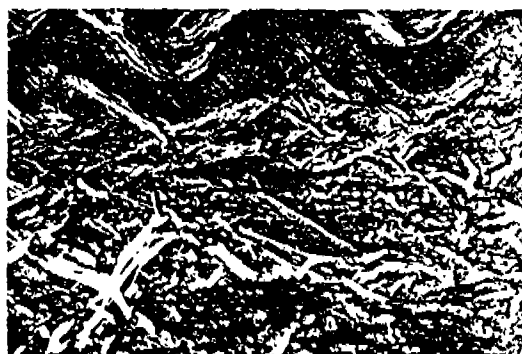


Fig 8.—Specimen of skin seen under polarized light. Note thickened bundles of collagen that appear bright yellow in color. Other collagen is less refractile (x250).

ness of the hands which progressed to discernible thickening. Concomitant with the above integumentary changes, other abnormalities, such as blanching and cyanosis of the skin associated with cold exposure, occurred. Within the few months prior to his clinic visit, the patient had been unable to extend his hands.

Abnormal physical findings were limited to the skin. There was thickening of the skin of all upper extremity digits with extension onto the dorsum of the hands, but sparing of the palmar surface. The hands blanched easily, but there was no evidence of cyanosis, clubbing, or telangiectasia. Upon extension of the hands, the fingers appeared claw-like. The patient was unable to completely extend the proximal and distal interphalangeal digits. Laboratory tests, skin biopsies, and further evaluation were declined by the patient.

Comment

Problems associated with the production of vinyl chloride and its polymers have been multiple and varied. Harris² described the vesicant action of vinyl chloride liquid when applied alone to the skin. It produces a second-degree burn that heals within two weeks when properly cared for. Danziger³ reported two deaths in autoclave cleaners due to asphyxiation while cleaning polymerization reactors after termination of the polymerization process. McCord,⁴ in a recent editorial, briefly notes the death of a woman worker in the plastics industry who, after exposure to molten polyvinyl chloride and methyl chloride cooling, developed acroosteolysis or a clinical picture that simulated the findings of scleroderma.

This, incidentally, is the only reported fatality of postpolymerization process acroosteolysis.

Vinyl chloride ($\text{CH}_2\text{-CHCl}$) is a colorless gas at room temperature with a boiling point of -13.9°C and a freezing point of -154°C . It has a very pleasant odor which can be detected in concentrations greater than 400 parts per million. In a gaseous state, it is highly flammable and explosive, its flash point being -78°C . In the late 1940's, its properties as a general anesthetic were studied; however, it was found to have dangerous myocardial irritability-inducing properties at narcosis levels.⁵ For three or more decades, the chemical (plastics) industry has used polymerized vinyl chloride to manufacture plastics whose ultimate product may be

found as wearing apparel, food wrappings, dentures, phonographic records, floors and wall tiles, cable coatings, shower curtains, and hundreds of other basic products used daily in homes and industry.

Polyvinyl chloride of varying molecular weight can be produced from vinyl chloride with the use of four basic methods and multiple minor modifications. In the more widely used process, deionized water, polyvinyl alcohol, methyl cellulose, gelatin, emulsifying agents, surfactants, buffers, trichloroethylene, catalysts (organic peroxides), and vinyl chloride in liquid form are agitated and heated in the absence of oxygen in a glass-lined autoclave or reactor. After 10 to 16 hours (the length of time determining the extent of polymerization and molecular weight of the finished product), the reaction is terminated. The finished product of the reaction is collected in a tank; impurities, including vinyl chloride, are extracted. The resultant polyvinyl chloride, when dried, is a mass of tiny particles of varying sizes, all of which are inert. The material is then bagged for shipment to fabrication plants.⁷

All of the processing up to the bagging stage is carried out in a closed system. Most plants have elaborate ventilating systems that automatically and continuously exchange room air when the concentration of vinyl chloride reaches a predetermined level.

After the polymer has been extracted from the autoclave, it is necessary to clean the reactor before the next run. (Some plants clean after several runs.) In order to clean the reactor, one or more workmen are required to hose the tank down with water; this is usually done from an external position. After hosing, workmen enter the autoclave to remove a thin film of the polymer which always remains on the reactor wall. This material, the exact composition of which is unknown, is thought to contain vinyl chloride (its odor can be detected), a quantity of the surfactants, catalysts, emulsifiers, and other substances, along with incomplete polymers of vinyl chloride.

Performance of this particular procedure (reactor cleaning) is the only one that has been found to be common to all persons so far observed who suffer from occupational acroosteolysis.

Dinman et al reported 25 cases, after an extensive survey of the factors involved in the development of occupational acroosteolysis in 32 plants, and noted that all except one of the patients had worked as reactor cleaners; the one exception, a laboratory worker, had cleaned laboratory reactors.⁸

Bagging is another task that has been found to be commonly associated with this disease. However, all baggers have been reactor cleaners at one period of time during their employment in the production of polyvinyl chloride. It is well to emphasize here that no cases have been observed in individuals working with vinyl chloride, the finished polymer polyvinyl chloride, its copolymers, or in processing the polymer into finished plastic products.

These findings have led most observers to conclude that one or more of the incomplete products of polymerization is responsible for the disease entity, occupational acroosteolysis.

Occupational acroosteolysis, first described by Suci et al in 1963,¹ can best be described as a symptom complex consisting of a Raynaud's-like phenomenon, involving the hands, sclerodermoid-like changes of the skin of the hands and forearms, and osteolytic and sclerotic lesions of the bones, particularly the extremities and sacroiliac joints. This induced combination is unique, and to our knowledge is limited to those individuals, specifically to "polycleaners" (reactor cleaners) in the vinyl chloride polymerization industry.

There are no accurate data which will give us a true incidence of the disease. Wilson observed 31 cases in 3,000 personnel involved in vinyl chloride manufacture and polymerization.⁹ Dinman et al reported 25 definitive cases in 5,011 employees in 32 plants throughout the United States and Canada.⁸ Sixteen other individuals were considered sugges-

tive but not definitive cases. Our two cases occurred in a plant which is considered small by industry standards, employing less than 100 persons in the manufacture of vinyl chloride polymers. More than these two cases may exist in the same plant, since one of our patients alluded to the occurrence of similar physical findings in at least one other supervisory person. We feel that it is well to add here that the health safety practices in this plant are at or above the norm for this particular industry.

The symptom complex of occupational acroosteolysis clearly points to the systemic nature of this disease. In most cases, affected individuals have a complaint of discomfort, i.e. tingling, burning, pain, and tenderness on exposure to cold, accompanied by redness, blueness, and blanching. This may occur in one or both hands. Later a diffuse swelling of the affected part or parts is noted. This is accompanied by difficulty in flexing or completely closing the hands. Clubbing of the fingers has occurred in some individuals. Although roentgenographic evidences of bony lytic lesions in the hands may be present early in the course of the disease, the affected individual usually has no symptoms or complaints referable to these. In a small number of cases, lytic lesions of the bones occur without evidences of a Raynaud's-like phenomenon. The period of exposure to vinyl chloride polymerization before the onset of symptoms is variable, as short as one month or as long as three years. Other associated symptoms as intermittent transient orthostatism and tinnitus are described but are difficult to attribute to the disease.

The physical findings in the affected parts, at first glance, simulate to a marked degree those of atherosclerosis. The hands are pink to blue to pale in color. The skin of digits and of the entire hand is thickened in a waxy and diffuse manner. In the early stages, thickening of the skin of the hands and wrists is most noticeable over the extensor and flexor tendons. This thickening is sclerodermoid in appearance and, when incomplete

as a rope-like or plaque-like quality to it. The skin in areas of diffuse thickening cannot be moved or caused to glide over subcutaneous tissues. Langer's lines may be absent in affected areas. The most striking difference in the clinical appearance of this lesion and scleroderma is the presence of functioning skin appendages and the absence of polygonal telangiectases in areas of active disease. In areas where ropy or plaque-like lesions are noted, the skin takes on a yellowish cast. In extensive cases plaques may extend up to and include the skin covering the entire forearms. Skin changes without a Raynaud-like picture may be noted in the feet.

Abnormal results from laboratory studies are practically nonexistent. None of the laboratory abnormalities usually associated with systemic scleroderma are present in patients affected with occupational acroosteolysis.

Abnormal x-ray findings indicating lytic lesions in various developmental stages are present in all cases of occupational acroosteolysis. These lesions are generally limited to the distal phalanges of the hands, ulna, radius, and sacroiliac joints. Early in the course of the disease, marginal and/or cortical defects occur. There is a loss of the cortex in one or more of the tufts of the distal phalanges. Later half-moon defects or cuts in the cortex of the tufts of the distal phalanges are noted. In the most advanced stages of the disease, the lytic lesions progress to cause transverse defects or fractures, and then complete resorption of the tufts and shafts of one or more distal phalanges. Involvement of the larger bones in the upper extremities may be evident in the advanced stages with cystic lesions and increased radiolucency becoming quite prominent. Extensive erosive and sclerotic

changes are also noted in the sacroiliac joints.

Oddly enough, in spite of the extensive destruction of bony structures, there are no symptomatic complaints referable to the musculoskeletal system. As evidenced by the progression of bony disease in our first patient, this process of destruction can continue for an as yet undefined period even after the patient has been removed from the causative environment. (There appears to be no accompanying progression of the skin lesions on termination of exposure.) His employment as a reactor cleaner was terminated immediately upon diagnosis of his condition in February 1970. His initial x-ray films of Feb 26, 1970 were rather unremarkable except for a transverse defect in one digit. One year later, Feb 16, 1971, nearly all of the digits of both hands were damaged, and defects in the left humerus were now present. X-ray films of the affected bones in the reparative stage show sclerosis in the region of transverse defects with the eventual result of bony union with digital shortening. In some cases, fragmentation of tufts predominates with resultant fibrous union and fragmentation.

The histologic examination of defective skin in case 1, although incomplete, demonstrated evidences of the disruption and fragmentation of old collagen, and fragmentation of elastic fibers with evidences of new collagen formation throughout the dermis. The epidermis and dermal appendages were not involved. These findings in most part are in accord with those reported by Harris. However, we were unable to confirm the presence of vascular involvement, ie, intimal fibrosis and medial hypertrophy.¹⁰ This preliminary evidence indicates that in this process the defect in the skin occurs solely in the connective tissue; a similar situation

probably exists in the connective tissue of bone, thus accounting for the type of bony defect described from x-ray examination.

Wilson⁹ believes the condition to be a combination of three factors: (1) a chemical insult, (2) a physical insult, and (3) personal idiosyncrasy because of the relatively low incidence (less than 3% of all production employees who had at one time reactor cleaning experience).

Treatment for this entity is nonexistent to date. Removal of the affected individual from the environment is so far the only known preventive. The skin disease is thought to stop its progression after exposure is terminated; however, it is evident that bony disease continues for an indefinite period of time, eventually terminating in one or more obvious bony defects.

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References

1. Suci I, Drejman I, Valeskal M: Investigation of the diseases caused by vinyl chloride. *Med Intern* 15:967-978, 1963.
2. Harris DK: Health problems in the manufacture and use of plastics. *Brit J Industr Med* 10:255-268, 1953.
3. Danziger H: Accidental poisoning by vinyl chloride. *Canad Med Assoc J* 82:828-830, 1960.
4. McCord CP: A new occupational disease is born. *J Occup Med* 12:234, 1970.
5. Patty FA, Yant WP, Waite WP: Acute response of guinea pigs to vapors of some new commercial organic compounds. V. Vinyl chloride. *Public Health Rep* 45:1963-1971, 1930.
6. Oster RH, Carr CJ, Krantz JC: Anesthesia: XXVII. Narcosis with vinyl chloride. *Anesthesiology* 8:359-361, 1947.
7. Cook WA, Giever PM, Dinman BD, et al: Occupational acroosteolysis: II. An industrial hygiene study. *Arch Environ Health* 22:74-82, 1971.
8. Dinman BD, Cook WA, Whitehouse WM, et al: Occupational acroosteolysis: I. An epidemiological study. *Arch Environ Health* 22:61-73, 1971.
9. Wilson RH, McCormick WE, Tatum CF, et al: Occupational acroosteolysis. *JAMA* 201:577-581, 1967.
10. Harris DK, Adams WGF: Acroosteolysis occurring in men engaged in the polymerization of vinyl chloride. *Brit Med J* 3:712-714, 1967.

ACRO-OSTEOLYSIS IN PVC WORKERS*

C. T. GITSIOS, M.D.

Esso Pappas

Polyvinyl chloride (PVC) is a widely used synthetic resin. It has been manufactured commercially for over 35 years and is used in upholstery fabric, floor and wall tile, wire insulation, phonograph records and many other commonly used commodities. For many of these uses, the resin is mixed with other materials to achieve the desired physical characteristics.

Basically the manufacture of polyvinyl chloride is accomplished by polymerization of vinyl chloride monomer. The process consists, briefly, in submitting a mixture of liquid vinyl chloride and water in the presence of catalyst to the effects of heat in large pressure vessels known as reactors or polymerizers. This produces polyvinyl chloride in slurry or latex form which is discharged from the vessel and conveyed elsewhere to be dried into a fine white powder. When the reactor is emptied at this final stage a deposit of white polymer is found on its inner wall. Air is then blown through the open vessel for at least a quarter of an hour, after which an atmospheric test for vinyl chloride is performed inside it. If the reactor is found to be clear of vinyl chloride vapor (below the acceptable TLV, 50 ppm), the cleaner enters it to clean the wall. The most common practice has been to accomplish the cleaning manually by using hand scraping techniques, with workers spending several hours each day on this job assignment. Personnel performing this job are commonly referred to as "polycleaners".

In the past five years attention was brought to a new occupational disease which appeared in people engaged in vinyl chloride polymerization process. This was almost simultaneously reported in Europe and the United States. Cordier et al¹ in France in 1966 first described an unusual condition which occurred in two men employed as polycleaners. After doing this work for several months these employees developed symptoms resembling those of Raynaud's phenomenon and later, a skin eruption of the hands and in one case in the forearms, together with general asthenia and drowsiness. The most striking sign, however, was the radiological evidence of lysis of

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some terminal phalanges of the hands, and in one case of the feet. Most of these abnormalities disappeared and the bones showed signs of healing a year or two after the men had stopped work. The name of acro-osteolysis was given to this disorder. About a year later Harris and Adams (1967)² from Imperial Chemical Industries Ltd., plastics division, described two similar cases in persons engaged in polymerization. About the same time Wilson et al (1967),³ from the medical department of Goodrich Co., reported a detailed analysis of 31 cases of occupational acro-osteolysis observed among 3,000 workers involved in vinyl chloride manufacturing and polymerization. The great majority of these cases have been characterized by two common factors, namely, (a) symptoms like those ascribed to Raynaud's phenomenon, and, (b) acro-osteolysis of the distal phalanges. A few had no symptoms but had the x-ray evidence of acro-osteolysis. Several of the patients had external skin lesions on the dorsal surfaces of the hands and forearms with a rope-like appearance resembling changes sometimes seen in scleroderma. Some had clubbing of the fingers. It is worthwhile noting that only a few of the above cases have sought medical attention because of symptomatic complaints (soreness and tenderness of the fingertips and marked discomfort on exposure to cold). The majority have been found through x-ray examination of the hands.

The above authors went further as to classify the positive x-ray findings into 3 stages according to the degree of the damage found.

In an early stage the main finding was a loss or a small halfmoon cut in the cortex of the tuft in one or more of the distal phalanges without destruction of the bone. In the 2nd stage there may be a more severe lytic destruction with complete loss of the tuft and a portion of the shaft. In the 3rd stage there is often definite fragmentation of the remaining tuft. During the healing stage this may go on to a complete bony union or remain as a fibrous union with fragmentation.

From an epidemiological point of view it appears that the job assignment seems to be the only correlation found so far with the occurrence of this syndrome. In general the syndrome has a low attack rate. In the experience of Wilson et al.³ it occurs in less than 3% of all production employees who at one time had polycleaning experience. It appears also that none of the cases in which the syndrome appeared had less than 12 months polycleaning experi-

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ence. It is believed by Wilson et al. that the condition is the result of three factors all of which must be present for occurrence: (1) a chemical insult, (2) a physical insult, (3) a personal idiosyncrasy. The *chemical* insult could occur from one or more of the monomers, catalysts and/or intermediate reaction products existing in polymerizers. A low degree of exposure to these could occur from contact with the solid, slightly moist, residue in the polymerizer or to small quantities of vapor, absorbed either percutaneously or by inhalation. The *physical* insult is present in all "polycleaners" to some degree through the prolonged hand scraping operations as well as the occasional use of hammers to remove the residues. *Personal idiosyncrasy* appears to be an important factor because of the low incidence of occurrence of the disorder and because of the fact that although all polycleaners are subjected to essentially similar chemical and physical insults, relatively few of them develop the disorder.

A point of general interest is the possible relationship of this condition to collagen disease. One patient of Harris and Adams (1967) two cases, had in fact, been diagnosed as a case of scleroderma on clinical grounds 10 years previously. Cordier et al. (1966)¹ mentions an unusual skin condition seen in their cases. Several of the cases of Wilson et al. (1967)³ also had external skin lesions on the dorsal surfaces of the hands and forearms. Finally Suciú et al. (1963)⁴ in a paper describing conditions produced by vinyl chloride also referred to a skin lesion resembling scleroderma, but acro-osteolysis was not mentioned.

Epidemiological Study

Late in 1966 after the first information about occupational acro-osteolysis became available, the Manufacturing Chemists' Association arranged with the University of Michigan to carry out a large epidemiological study both for the MCA and for the industry. This study was carried out in the vinyl chloride industry and included questionnaires, x-ray examinations of the hands, job history and industrial hygiene studies. There were 5011 employees in 32 plants of 19 corporations in the United States and Canada in the survey. Controls totalling 2407 were drawn from the Tecumseh, Michigan, epidemiologic study. Of the 5011 workers, 1302 were found to have an x-ray abnormality of the hands. Most were found to be unrelated to acro-osteolysis. The roentgen findings were correlated with the

history of Raynaud's phenomenon, and diagnostic categories established. Raynaud's phenomenon and characteristic x-ray changes establish the diagnosis of acro-osteolysis. An additional category involves severe roentgen changes of several fingers and is believed to represent the end stages of the disease.

The investigators established a total of 25 cases with an additional 16 "possibles" in whom x-ray changes were seen but Raynaud's phenomenon was not. The ratio of patients with clinical disease to those exposed to the chemical hazard was 1:31.

Esso Pappas PVC Operation

Esso Pappas has operated a PVC plant since early 1967, with a work force of about 35 persons. Our PVC plant consists of 8 reactors and was originally designed to produce 12,000 metric tons/year. It is a batch operation and the vinyl chloride monomer used in the process is received through pipeline from the supplier. During the past 18 months after continuing experiments in improving PVC processing, a capacity of 20,000 mt/year was reached.

Figure 1 is a view of the reactor room. The reactors are installed in two rows. The greater part of the 5.5 meter long reactor lies below the floor as you can see in Figure 2.

Figure 3 gives you an idea of the shape and the dimensions of each reactor.

After the process is completed the product is transferred from the bottom of the reactor to the finishing section where it is dried, screened and then fed into a bin for subsequent bagging.

Figure 4 shows a close up view of the reactor.

Although the materials of industrial hygiene concern in PVC production include vinyl chloride, methanol, catalyst, bisphenol A, carbon monoxide and PVC dust, vinyl chloride monomer seems to be the most important.

Since the polymerization operations are carried out in closed process, this provides little opportunity for employee exposure. The first industrial hygiene survey done by ER and E group on Dec. 1967 demonstrated that during normal operations the level of vinyl chloride throughout the plant is relatively low.

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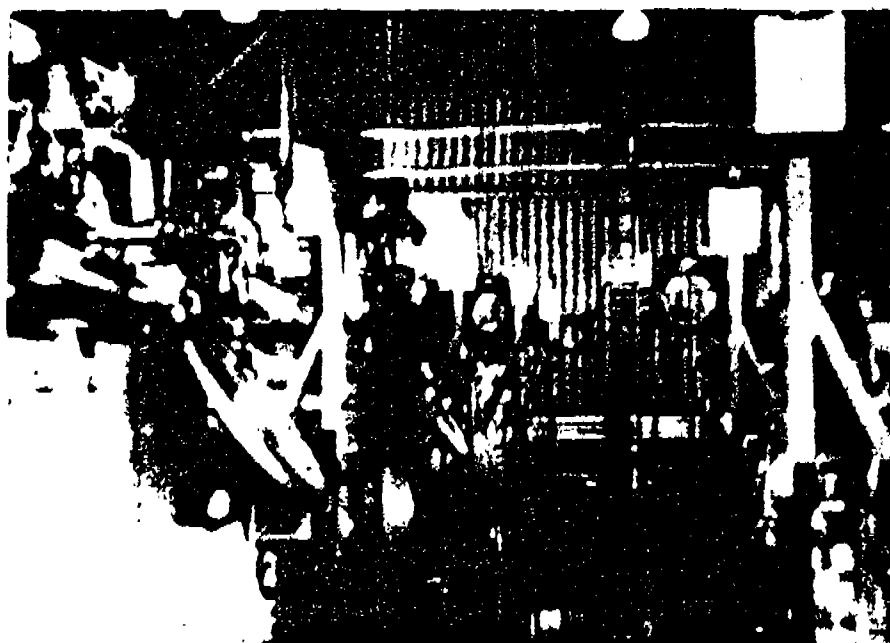


FIGURE 1 - PVC REACTOR ROOM



FIGURE 2 - LOWER PART OF PVC REACTORS

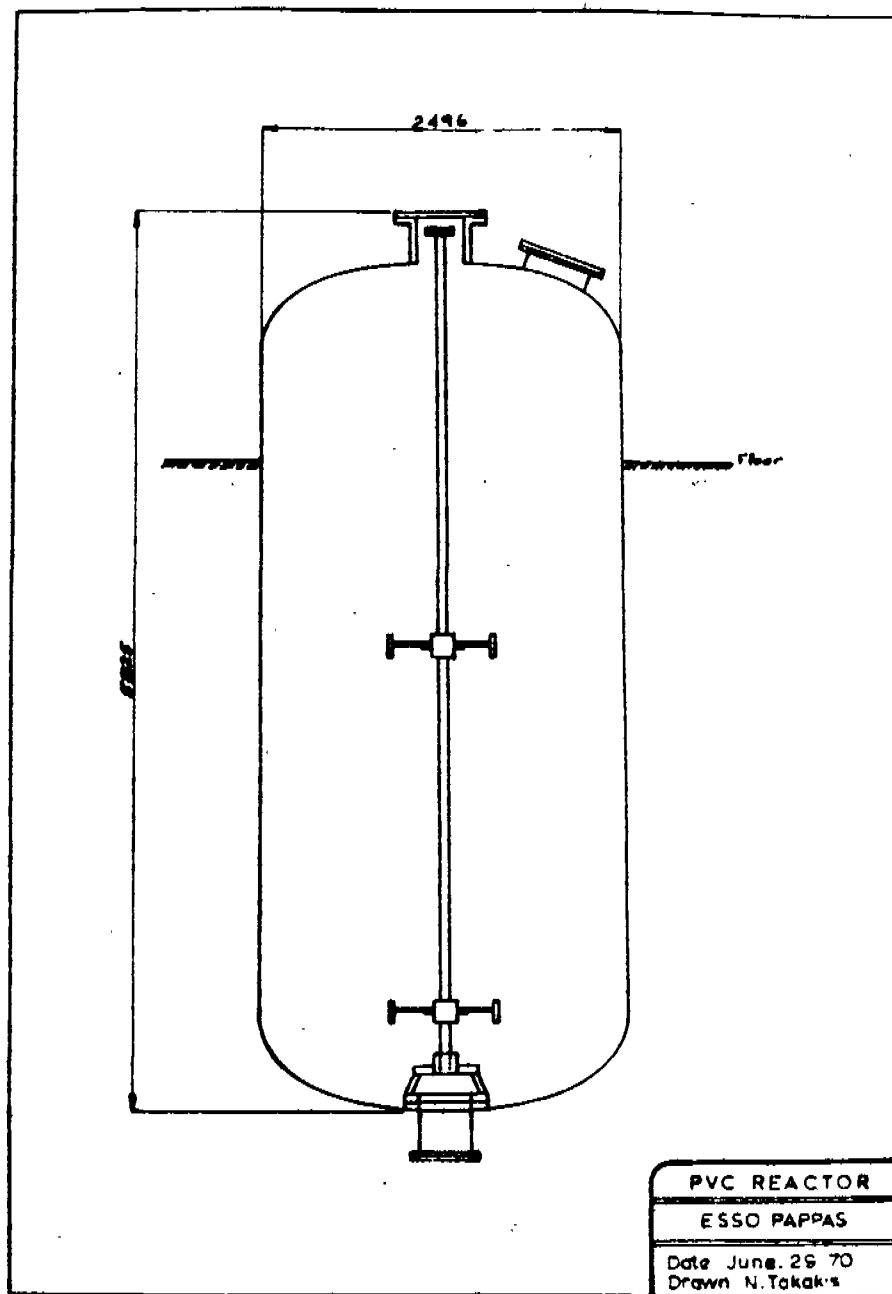


FIGURE 3

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There were stages in the production process, however, which resulted in brief exposure to high concentrations, for example: (a) During the addition of water to the reactors the air displaced from the reactor contained as much as 10,000 ppm of vinyl chloride. This was due to a leakage at the manual control valve on the vinyl chloride monomer feed line and was corrected. (b) Vinyl chloride monomer was released to the workroom when the reactor was opened to obtain a sample of the PVC following completion of the reaction. (c) Polymer removed from the reactors following cleaning was originally placed in open waste drums. The concentration of V.C.M. in these drums was as high as 600 ppm. This was a source of airborne contamination and was eliminated by covering the drums and emptying them at the end of each shift.

Following transfer of the product from a reactor to the finishing section the reactor is washed out with water and following this an air mover is attached by flexible duct to the reactor discharge outlet and operated until the concentration of V.C.M. inside the reactor is 50 ppm or less. This determination is made by using colorimetric

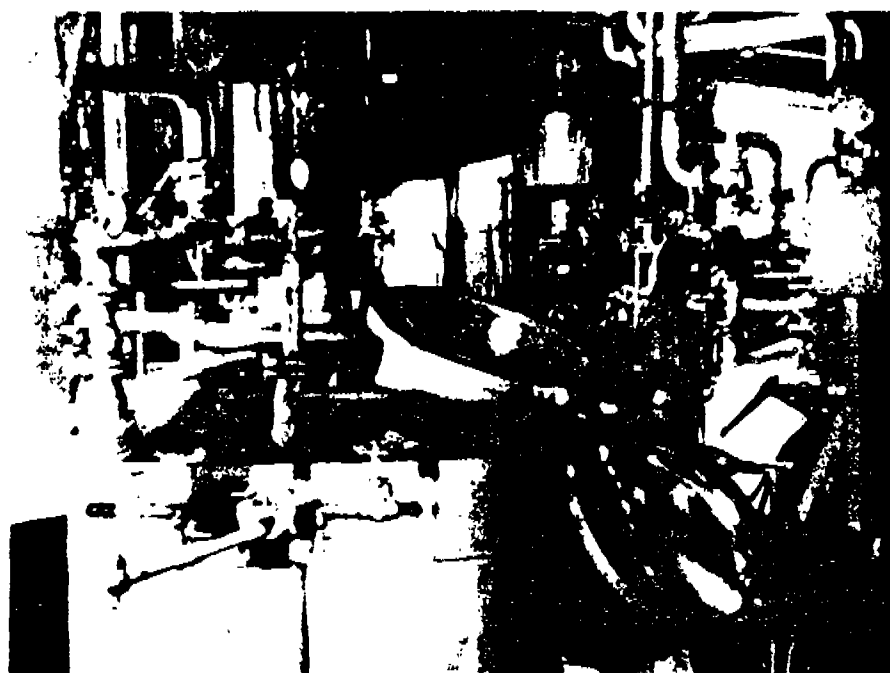


FIGURE 4 - TOP OF PVC REACTOR - ENTRY HATCH OPEN

detector tubes. Entry of the technicians for cleaning is not permitted until this level is reached. Reactor clean-out men are supposed to wear coveralls (plastic-coated or neoprene), work gloves and hard hats during this procedure.

Following the ER and E hygiene inspection the recommendation was made that neoprene gloves should be used by the polycleaners because through experiments it was found that this type of gloves was less permeable to V.C.M. In practice, however, these gloves were not found satisfactory for two reasons. First, they would tear easily, so that most of the time the gloves had holes and secondly, they were very uncomfortable to the technicians whose hands at the end of a reactor cleaning session were moist and the skin wrinkled. As a consequence the technicians were happy to see the gloves being torn and were not eager to change them. It was obvious that in this way the protection they were getting was minimal, if any, and so we had to return to the old canvas type work gloves. After all some protection was better than none.

In addition to the industrial hygiene measures outlined we have established the following program of medical check-ups for all people engaged in PVC production, testing and handling:

1. Yearly x-ray's of the hands.
2. A yearly periodic examination.

Up to this time we have had no abnormal x-ray findings nor have there been any clinical findings related to the above disorder.

References

1. Cordier, J. M. et al: Acroosteolysis et lésions cutanées, associées chez deux ouvriers. Affectées au nettoyage d'autoclaves. Cah. Med. Travail 4: (Jan.) 1966.
2. Harris, D. K. and Adams, W. G. F.: Acro-osteolysis occurring in men engaged in the polymerization of vinyl chloride, Brit. Med. J. 3:712, 1967.
3. Wilson, R. H. et al: Occupational Acroosteolysis, J.A.M.A. 201:577, 1967.
4. Suciu, L. Drejman J. Valaskai, M: Contributii Studiul Imolnavirilor Produce de Clorura de Vinil. Med. Intern. 15:967, 1963.

Occurrence of Alkylmercury Compound in Caustic Soda Factory

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A compound resembling methyl mercury has been found in the area surrounding a caustic soda factory where only metallic mercury has been used in the manufacturing process. Most of methyl mercury occurs in the sludge of a treatment pit for effluent water that contains inorganic mercury. Chemical characteristics identifying the physical properties and toxicity of the compound all indicate the probability that the substance is methyl mercury.

MINAMATA disease has furnished tragic illustration of the danger of environmental pollution that may follow upon rapid and improvident industrial development. Studies of acceptable limits of mercury in biological and environmental milieus¹ disclose several problems which urgently call for clarification.

It is established that fishes caught in a natural environment contain a certain amount of methyl mercury,² though knowledge of the origin and potential toxicity in these circumstances is still insufficient. From the viewpoint of public health, an evaluation of the biological significance of methylmercury as it appears in the food chain is imperative.

This article describes recovery of an alkylmercury compound from the sludge pit of a caustic soda factory in which only metallic mercury has been used in the electrolysis of sodium chloride. The compound has chemical and toxicologic properties that seem to

identify it as methyl mercury. This is the first available evidence for alkylation of organic mercury in an apparently inorganic system.

Measurement of Mercurials in Caustic Soda Factories

Samples of water and of sludge were collected at several sites at two factories. Measurement of total mercury has been carried out by cold-vapor atomic absorption method.³ Identification and determination of alkylmercury have been done by gas chromatography and thin-layer chromatography.^{4,5} The results obtained are shown in Table 1.

Chemical Production of Substance X (Methyl Mercury) in an Inorganic System

To confirm the production of methylmercury chloride in the process of electrolysis of sodium chloride or thereafter, the following experimental studies were carried out:

1. Measurement of methylmercury chloride in water containing metallic mercury.
2. Measurement of methylmercury chloride in mercury bichloride (mercuric chloride) solution.
3. Measurement of methylmercury chloride in a solution of inorganic mercury (mercury bichloride, mercuric sulfate) mixed with activated carbon (carbon black, a mixture of carbon and acetylene carbon black) (Fig 1, top).
4. Measurement of methylmercury chloride in a solution of inorganic mercury (mercury bichloride, mercuric sulfate) mixed with calcium carbide or calcium chloride (Fig 1, bottom).

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A substance resembling methyl mercury was found in the last two years.

Fig 1. Mercury chloride experiment 4.

Synthesized substance

Authentic

(Small peak number)

A

B

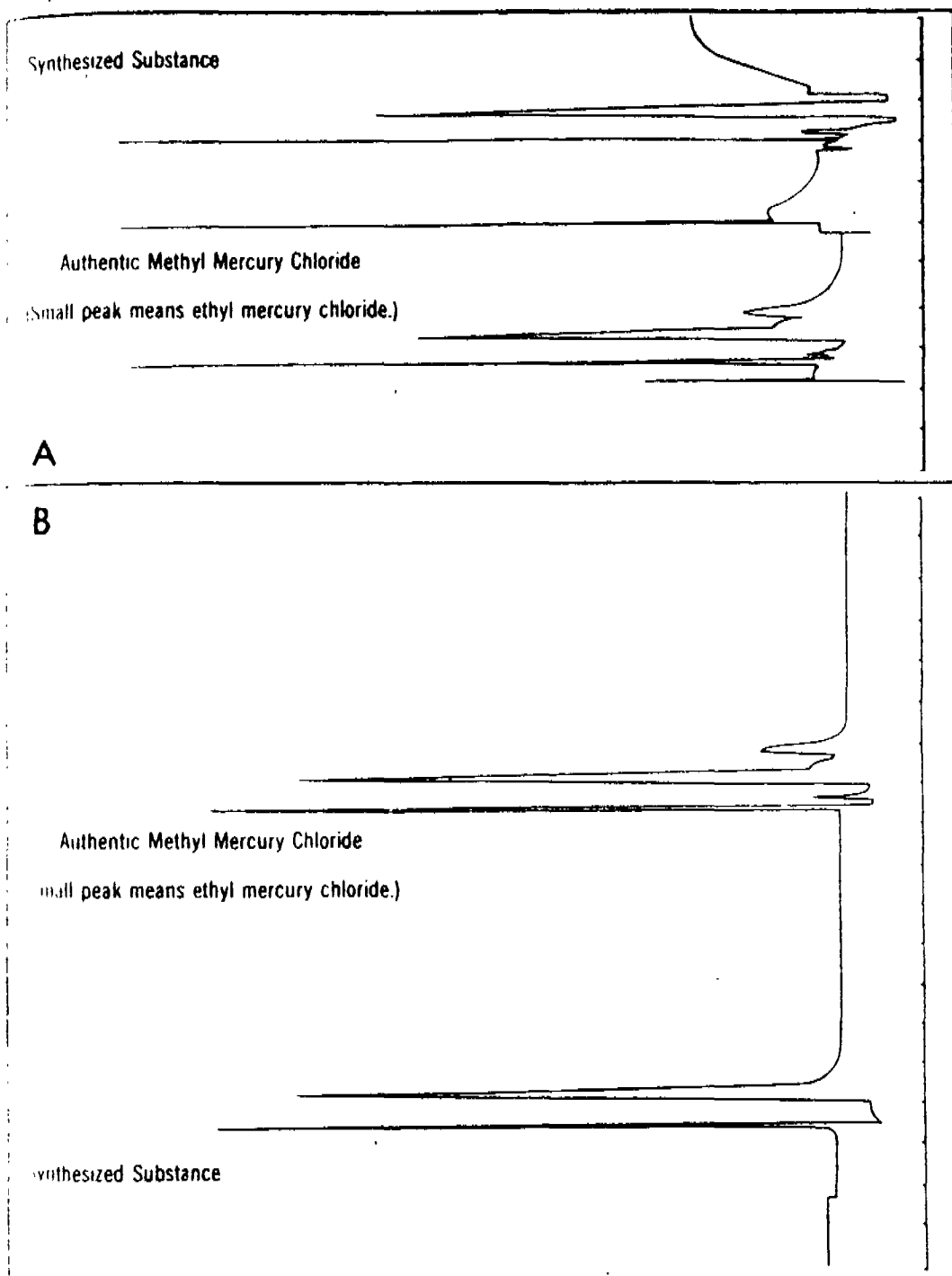
Authentic

(Small peak number)

Synthesized

A substance similar to and thought to be methyl mercury chloride was recognized in the last two experiments (3 and 4). The production of a similar substance thought to be methyl mercury chloride was also identified in effluent water from the electrol-

Fig 1.—Retention times of two experimentally synthesized substances and authentic methyl mercury chloride. Top, Synthesized substance of experiment 3. Bottom, Synthesized substance of experiment 4.



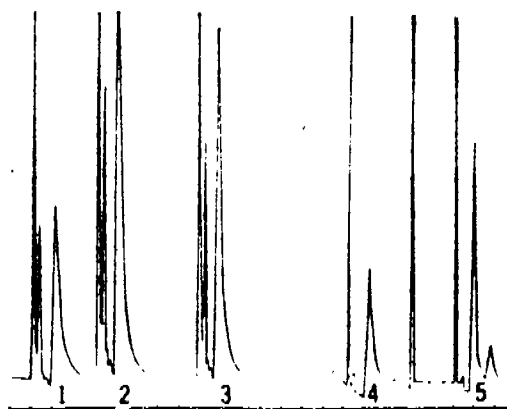


Fig 2.—Retention times of a similar substance produced in effluent water and authentic methyl mercury chloride. 1, 2, and 3 are the substance produced; 4 and 5 are authentic methyl mercury chloride.

ysis plant when calcium carbide or its precipitate was added and mixed with the effluent. The retention time of the product measured by gas chromatography (Fig 2) corresponded to that of methyl mercury chloride.

Crystallization and Chemical Properties of Substance

The substance which was obtained in experiment 4 was collected and crystallized by the method shown in Fig 3. All reagents were carefully checked in advance to eliminate contaminants. The crystalline material

obtained methyl mercury chloride at 1°C. The absorption spectrum of the substance showed a maximum at 254 mμ, which is characteristic of methyl mercury chloride. The substance responded to the R₁ test for mercury. The crystalline material was developed on the R₁ test for mercury. The substance was found to be methyl mercury chloride.

Fig 3.—Method of extraction and crystallization of alkylmercury compound.

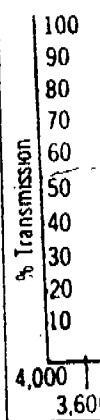
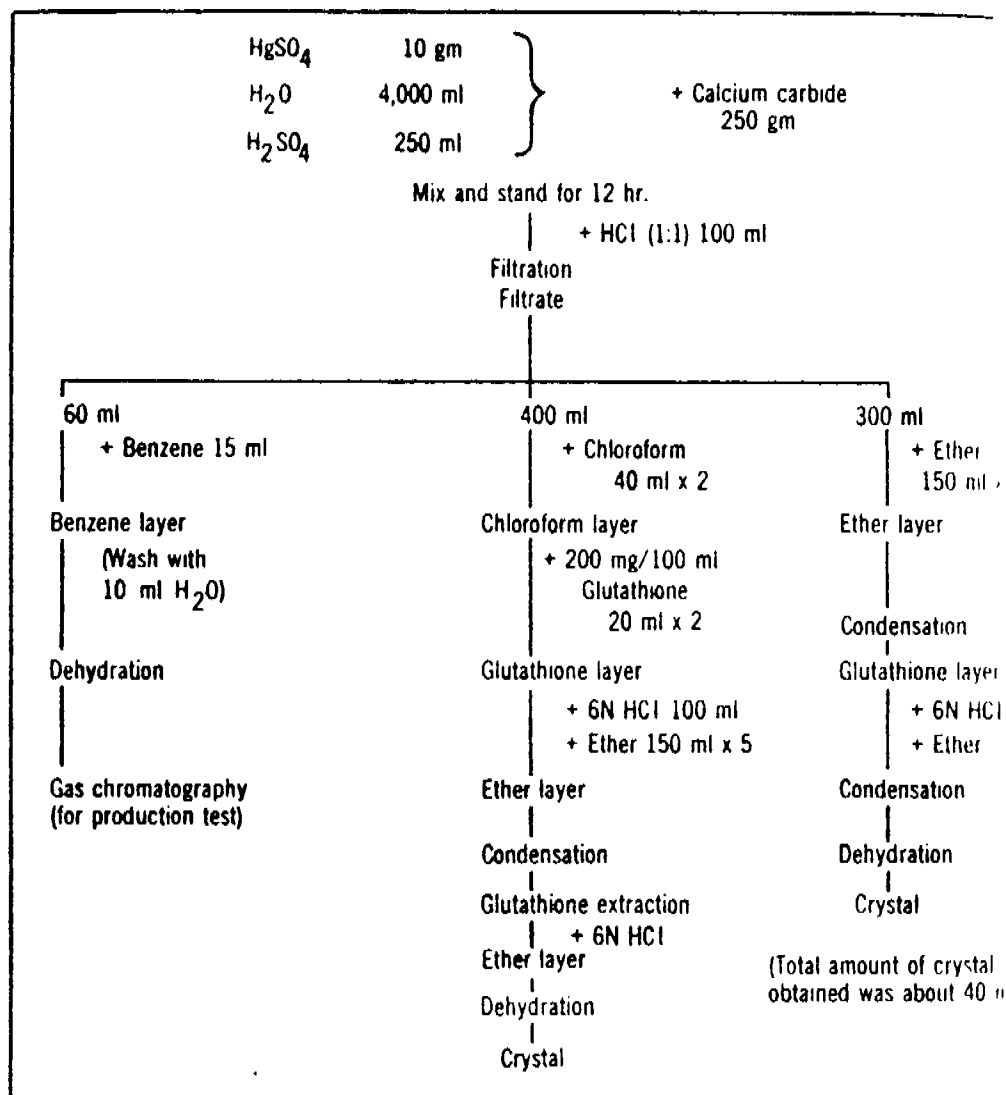


Fig 4.—Methyl mercury chloride.

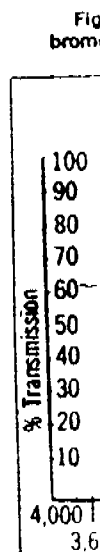


Fig 5.—Bromine.

obtained had the characteristic odor of methyl mercury chloride, melted and evaporated at 173°C, and had 788 cm^{-1} and 1,190 cm^{-1} absorption by infrared analysis as shown in Fig 4. These findings almost correlated with those of authentic methyl mercury chloride (Fig 5). A solution of the crystalline material was spotted and developed on a thin-layer chromatograph, and the portion was scraped off and analyzed for mercury by the cold-vapor atomic absorption method. The locus where mercury was found showed the same R_f value as that of methyl mercury chloride.

Toxicological Identification of Crystalline Substance

The characteristic symptoms of methyl mercury chloride poisoning in the rat are ataxia and crossing of the hind legs when the rat is hung by the tail with the head down. The crystalline material was dissolved in water with the aid of propylene glycol and administered subcutaneously to rats once every two days (except Sundays) in a dose of 0.5 mg/day. The total amount of the crystalline material administered to the rat was 13 mg by the end of the experi-

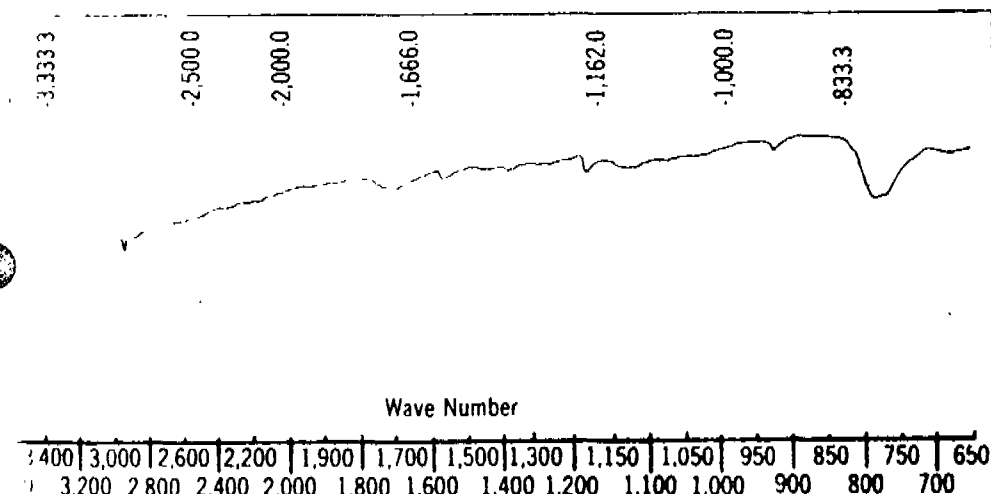
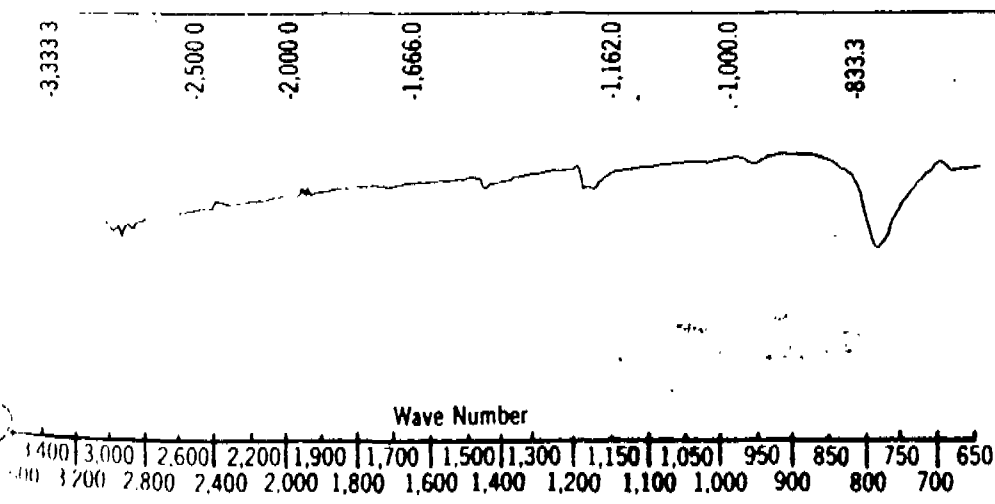


Fig 4.—Absorption of synthesized substance by infrared analysis, using potassium bromide-disk method.

Fig 5.—Absorption of authentic methyl mercury chloride by infrared analysis, using potassium bromide-disk method.



Total Mercury and Methyl Mercury Chloride Found in Effluents From Two Caustic Soda Factories

Factory A			
Sample	Total Hg, ppm	Methyl Mercury Chloride, ppm	Total Hg, ppm
Electrolysis plant			
Small pit (water)	4.17	ND*	4.90
Large pit (water)	4.13	ND	4.50
Large pit (sludge)	359.90	0.014	273.60
Effluent water			
(Water)	0.29	ND	0.04
(Sludge)	19.96	ND	16.12
Sedimentation pond			
(Water)	0.11	ND	0.05
(Sludge)	25.39	0.001	20.56
Calcium sludge depot	28.27	0.003	254.45

* ND, not detected.

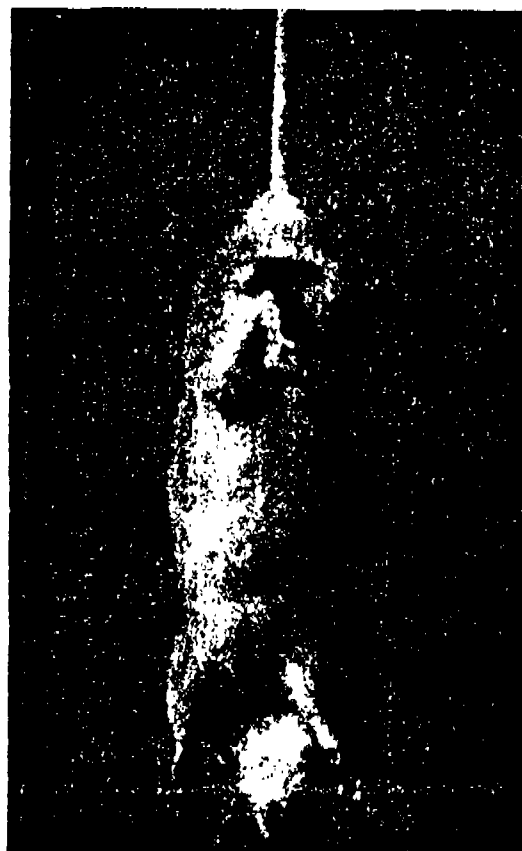


Fig 6.—Crossing of hind legs in rat which received authentic methyl mercury chloride.



Fig 7.—Crossing of hind legs in rat experimentally synthesized crystal

ment, ie, 30 days after the first injection.

Figures 6 and 7 show, respectively, the crossing of hind legs in rats which received authentic methyl mercury chloride and the crystal obtained experimentally. The normal leg reflex of a control rat which received

only propylene glycol is shown in Figure 8.

The rat was killed after the onset of ataxia, and the amount of methyl mercury chloride in various organs was determined. The following tabulation shows the results of methyl mercury chloride.



Fig. 1. Normal leg reflex of control rat.

1.5 million, found in the organs of a rat which the synthesized material was administered:

Brain	0.78
Liver	6.58
Kidney	33.40
Heart	1.68
	6.50
Stomach	1.12
Intest.	18.48

Comment

Several indications of occurrence of methyl mercury in a natural environment have been reported previously.⁶

The discovery that methyl mercury chloride may be produced in an inorganic system similar to that used industrially in caustic soda plants raises problems of major importance. In the industrial situation the reaction has occurred mainly in a sedimentation pit where a precipitate of calcium carbide is added to neutralize water from the electrolysis plant. These observations may indicate the main source of the methyl mercury in the effluent material from caustic soda plants.

This statement does not imply that other possibilities may be neglected. A trace amount of methyl mercury has also been produced experimentally in reaction of inorganic mercury with amorphous carbon—the material of which electrodes in the electrolysis plant are fabricated.

The demonstration of the possible production of methyl mercury in a commonly used inorganic process raises serious questions. These apply to both the amounts of methyl mercury produced in such a fashion and to the potential entry of this material into biological systems. If these processes occur, they may have significant effects on human health, especially if methyl mercury should enter the human food chain or if some biological forms concentrate the substance.

References

1. Berlin M: On estimating threshold limits for mercury in biological material. *Acta Med Scand* 173 (suppl 396):1-29, 1963.
2. Westö G: Determination of methylmercury compounds in foodstuffs: II. Determination of methylmercury in fish, egg, meat, and liver. *Acta Chem Scand* 21:1790-1800, 1967.
3. Yamaguchi S, Matsumoto H: Ultra microdetermination of mercury in biological materials by atomic absorption photometry. *Jap J Industr Med* 10:125-133, 1968.
4. Yamaguchi S, Matsumoto H: Ultra-micro determination of alkylmercury compounds by gas chromatography. *Kurume Med J* 10:33-42, 1969.
5. Yamaguchi S, Matsumoto H, Hoshida M, et al: Microdetermination of organic mercurials by thin-layer chromatography. *Kurume Med J* 10:53-56, 1969.
6. Wood JM, Kennedy FS, Rosen OG: Synthesis of methyl-mercury compounds by extracts of a methanogenic bacterium. *Nature* 230:173-174, 1968.

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PATHOLOGY OF VINYL CHLORIDE
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During the last years a syndrome characterized by alterations of the skeleton, teguments, nervous system and hepatic function^{1, 2, 3, 4, 5, 6} has been observed among the workmen associated with vinyl chloride polymerisation process. An experimental programme has been performed in order to evaluate the toxic effect of vinyl chloride on the animal organism, and in order to try to reproduce in rats the acroosteolytic lesions observed in man.

MATERIALS AND METHODS

Twenty-five Wistar male albino rats, of average weight 150 gr., were exposed to vapours of vinyl chloride 4 hours a day for 5 days a week during 12 months. The animals were kept in a plastic air-tight container through which there was a constant flow of air containing 3% in weight, equal to 30,000 p.p.m. of vinyl chloride. At the end of treatment the surviving animals were killed at twenty-day intervals, and the paws, brain, liver, kidneys and thyroid were examined histologically after fixation, inclusion and colouration by the ematoxylin-eosine. Van Gieson, PAS, Weighert, Bielschowsky-Gomori methods. Twenty five rats of the same breed were set aside as a control.

RESULTS

During the period of exposure the animals were slightly soporific, but the first few months of treatment were well tolerated and the rats showed no change in body growth or behaviour and no organic alteration visible macroscopically or by radiological means. After ten months some of the animals began to show a decrease in weight, in aggressiveness, in their reaction to external stimuli, and often a disturbed equilibrium. Thirteen animals died from cardio-respiratory complications. Two animals died from hemato-peritoneum. Most of the animals showed pathological involvement

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of the brain, liver, kidneys, and thyroid. Six rats showed histopathological alterations of the skeleton.

The small metatarsal bones showed an extensive periosteal proliferation of cartilage-like material apparently originating by metaplasia directly from the bone. All around the newly formed cartilage the cellular components were compressed and arranged tangentially to the cartilage itself, forming a perichondral layer. The isogenous cartilagenous groups were irregularly arranged and their nuclei were of varying size and often number per cell. The edges of the cartilage were irregular, showing digital extroflexions resulting from a varying growth potential. There was also evidence of chondroid metaplasia in areas of mature compact bone, in which the cartilaginous elements were grouped around a central nucleus of bone, as in typical osteochondromatous processes. In the small bones the chondroid metaplasia was often very extensive and the bones seemed to be impregnated with a mucoid substance which altered the characteristic disposition of the bone tissue obliterating the cement lines. The skin of the paws showed areas of hyperkeratosis superficial thickening of the epidermis, vacuolization and degeneration of the basal layer, disappearance of the cutaneous adnexa and modest accentuation of the papillar layer of the derma. An almost constant state of edema was observed in the epidermic zone. The connective tissue showed dissociation of the collagen bundles and a diminution and fragmentation of the elastic reticulum. The small arterial vessels showed signs of endothelial fibrosis with a thickening and dissociation of the elastic membrane, often accompanied by a partial hyaline degeneration and homogenization of the walls and proliferation of the endothelium. Some of the vessels appeared completely blocked by a proliferation of the connective tissue in a formation not unlike that of onion skin.

The small nerve bundles were often surrounded and invaded by fibrotic processes. A microscopic examination of the brain revealed diffuse degenerative lesions of the grey and white matter. The external granular layer was often reduced and in some areas this was true also the medium sized and giant cells. Numerous examples were found of hypercoloured, atrophic neurons with disappearance of the nucleoli and sometimes also of the nucleus itself. At the level of the white matter there were zones of intense, reactive gliosis consisting for the most part of cytoplasmic and fibrillar astrocytes, some of which were arranged in a concentric disposition around the blood vessels. There was evidence of neuronal phagocytosis with satellitosis and the deposition of neuroglial elements around the altered nerve cells.

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There was modest proliferation of microglial elements, especially in areas of more intense gliosis and zones of intense spongiosis showing an accumulation of astrocyte-type elements with basophilic cytoplasm and abounding in gemistocytic and microglial elements similar in appearance to "scavenger" cells. The cerebellum showed signs of atrophy of the granular layer which was often represented only by a few isolated nuclei. The layer of Purkinje cells was in some places profoundly modified, the cells appearing to be undergoing intense degeneration and all the various stages of this process were observed, from the whole cell to the small homogeneous bodies with indistinct outlines which represent the most damaged form of the cell. Except for small and limited areas, the molecular layer seemed to be well preserved.

The liver was often of increased volume, sometimes subicteric in colour, with a smooth surface and somewhat more brittle consistency than normal. A histological examination showed in the majority of cases signs of diffused interstitial hepatitis with numerous hepatic cells in the grip of regressive processes varying from torbid degeneration of the cytoplasm to necrosis with marked cytoplasmic and nuclear polymorphism. Some of the hepatocytes showed giant or double nuclei. In these areas of cellular necrosis a corpuscular exudation was always present consisting of round cellular elements of the lymphocyte or plasmacellular type. There was evidence of an abnormal proliferation of the Kupffer's cells, which were often hypertrophic. The triangular spaces appeared to be increased by the infiltration of round and polynucleated cells and eosinophiles showing marked polymorphism. The portal capillaries, centrolobular veins and sinusoids were often blocked by numerous centrally-located areas of partial necrosis, often accompanied by a diffuse steatosis in the form of small drops with clearly-defined areas of acidophile necrosis and the formation of elements similar to the round acidophile bodies of viral hepatitis and the "Councilman" bodies of yellow fever. In certain cases evidence was found of an intense fibrosclerotic reaction alongside the degenerative processes.

The kidneys did not appear to be excessively altered by the prolonged treatment with vinyl chloride, although they showed signs of tubulonephrosis, sometimes accompanied by chronic interstitial nephritis.

The thyroid often showed a colloid goitre and a marked increase in parafollicular cells.

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The control animals showed no histopathological alterations of the skeleton or of the various organs.

CONCLUSIONS

This research confirms that the animals are sensitive to the toxic action of vinyl chloride. The lesions of the bone and connective tissue are similar to those noticed in experimental osteo-latyrim and to those described in a man affected with acroosteolysis of the hands (Marin). It should be pointed out that the roentgenological findings of skeleton in man rests on cartilaginous transformation of the bone tissue. Therefore according to recommendation made at XVI International Congress on Occupational Health of Tokyo (1969) I should like some precautions to be taken in the manufacturing plants polymerizing vinyl chloride, such as reduction of the threshold limit value of monomer, and substitution of manual cleaning of autoclaves by automatic devices.

SUMMARY

The results of this investigation show that animals exposed to vapours of vinyl chloride may show degeneration of the skeleton and connective tissue with histopathological pictures similar to those observed in human acroosteolysis of the hands. The bones in fact undergo processes of intense periostium growth and diffuse, chondroid metaplasia. The connective tissue is dissociated into collagen bundles with a reduced number of cells, the elastic reticulum is markedly reduced and fragmentary, the small vessels of the deep layers of the derma show hypertrophy of the walls with a diminution and sometimes obliteration of the lumen, the nerve endings are surrounded and infiltrated by fibrous tissue. Degenerative processes of the parenchyma were observed in the brain, in the liver and in the kidneys.

NOTE: Figures on available copy were not suitable for reproduction. They are as follows:

Fig. 1 -- Periosteal proliferation of metatarsal bone of a rat 16th months old, exposed to vinyl chloride vapours for 12 months

Fig. 2 -- Periosteal proliferation of metatarsal bone of a rat, 16th months old, exposed to vinyl chloride vapours for 12 months

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Fig. 3 -- Periosteal proliferation of metatarsal bone of a rat, 16th months old, exposed to vinyl chloride vapours for 12 months.

Fig. 4 -- Chondroid metaplasia in mature bone of metatarsus of a rat, 16th months old, exposed to vinyl chloride vapours for 12 months

Fig. 5 -- Chondroid metaplasia in mature bone of metatarsus of a rat, 16th months old, exposed to vinyl chloride vapours for 12 months

Fig. 6 -- Chondroid metaplasia in mature bone of metatarsus of a rat, 16th months old, exposed to vinyl chloride vapours for 12 months

CANCEROGENIC EFFECT OF VINYL CHLORIDE

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Presented at the Tenth International Cancer Congress
Houston, Texas May 22-29, 1970

The demonstration of oncogenic activity of some chemical organic compounds employed for the preparation of "plastics" has been widely investigated and the limits and the effectiveness of their oncogenic power have been well defined. The present investigation demonstrates that it is possible to obtain for some experimental models a marked carcinogenic response to a monomeric precursor, i.e. vinyl chloride, of plastic polymers which follows a peculiar pattern for different tissues and organs of the rat.

Twenty-six Wistar (AR/IRE) male albino rats, of the average weight of 150 gr. were exposed to vapours of vinyl chloride 4 hours a day for 5 days a week during 12 months. The animals were kept in a plastic, air-tight container through which there was a constant flow of air containing 3% in weight equal to 30,000 p.p.m., of vinyl chloride. At the end of treatment the surviving animals were killed at twenty-day intervals, and the most important tissues and organs were histologically examined by conventional methods. Twenty-five rats of the same strain were kept aside as a control. During the period of exposure the animals were slightly soporific, but the first few months of treatment were well tolerated and the rats showed no change in body growth or behavior and no organic alterations visible macroscopically or by radiological means. 65% of the animals developed tumors of the skin and 26% of these showed tumors of the respiratory tract exclusively localized in the lungs. Very few animals developed tumors in the bone and in this case the tumors were localized in the metaphysical region of the femurs, and it is worthy to mention that the femurs of both posterior limbs showed the carcinogenic transformation.

Tumors of the skin

The skin transformation which developed more frequently in the para-aural region, has been the epidermoid carcinoma, but we have seen also papillomas and rarely mucoepidermoid carcinomas.

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Tumors of the respiratory tract

Even if as far as the percentage is concerned these occur in a smaller number, their morphologic appearance is mainly of an adenocarcinoma; only in one rat it has been observed a tumor of the epidermoid type. Sometimes the tumor showed an early developmental stage and consisted predominantly of cubic or columnar cells arranged as regular or irregular tubular and papillary elements supported by poorly developed fibrous stroma.

Tumors of the bones

In the metaphysical region of the four limbs a large proliferation of cartilaginous tissue arises outwardly to the periosteum and seems to derive directly out of the osseous cortical by the growth of its cells. The cartilaginous growth is dishomogeneous as it is shown by the extension of finger-like prolongations into the boundary of neoformed tissue. Beside the chondroblastic, chondrocytic and angiomatous areas, manifestation of noticeable growth power, there are cartilaginous zones with regressive features, as fibrosis and hyalinosis.

The results reported above indicated that vinyl chloride is an effective carcinogenic agent for the rat. As for many carcinogenesis studies, where multiple tumors arise at different sites, in different tissues and organs, the data obtained need to be evaluated considering a more prompt positive response according to the ideal concentration of the carcinogenic. It is noteworthy to emphasize that the cutaneous system represents an impressive pattern of susceptibility to the vinyl chloride. Another point to be considered is that all the cutaneous tumors developed in the same site, i.e., the region including the area in which submaxillary and parotid gland are located.

No implications to human pathology can be extrapolated from the experimental model reported in this paper.

neumonia, and moderate swelling of the kidney parenchyma, often assuming the pattern of tubulonephrosis.

RESULTS

The rates of survival and the main findings are summarized in Table 1. Almost all the animals developed tumors of the skin and lungs. Very few animals developed bone tumors; in these cases, the tumors were localized in the metacarpal and metatarsal bones of all 4 extremities. Skin tumors were by far the most frequent, amounting to 65 or 70%.

Skin Tumors. The tumor that developed most frequently in the paracardiac region was the epidermoid carcinoma, but we also observed papillomas and rarely mucoepidermoid carcinomas. In all cases, the neoplasms were of epithelial nature. The 3 patterns noticed cannot be compared to various histotypes but rather to a transition of one type into the other, and which is more likely, to different stages of the same proliferative type.

Very significant papillomas occurred in some rats. The histological picture showed progressive epithelial proliferation, with progressive increase in the thickness of the epidermis (Fig. 1).

The papillary warts of exophytic type had a fibrous vascular stroma and various degrees of inflammatory lymphocytic infiltration, marked hyperkeratosis, parakeratosis, acanthosis, and areas of individual dyskeratosis or pearl-like horny formations.

The epithelial cells of the penetrating columns (Fig. 2) were irregularly arranged and were frequently accompanied by an inflammatory infiltration of the dermis. The typical features of the Malpighian layer and of the stratum corneum of the prickly cells and of germinal layers were easily recognized (Fig. 3). The horny layer was composed largely of cell nests, which appeared at certain points within the epithelial masses and assumed the well-known appearance of "horny pearls" (Fig. 3, arrows); they were made of flattened and compressed prickly cells without nuclei and were located around a central core of keratin.

Table 1
Oncogenic effects of inhaled vinyl chloride as a function of time

The animals were exposed to vinyl chloride vapors for 4 hr a day, 5 days a week, for a total of 12 months, in a constant flow of air containing 3% v/v vinyl chloride.

Rat	Survival rate	Tumors		
		Skin	Lungs	Bones
1	300	Mucoepidermoid carcinoma	Adenocarcinoma	Osteochondroma
2, 3	280-300	Epidermoid carcinoma, keratinizing type	No tumor	No tumor
4	310	Epidermoid carcinoma, keratinizing type	Adenocarcinoma	No tumor
5	333	Papilloma, keratotic type	No tumor	Osteochondroma
6	337	Epidermoid carcinoma	No tumor	Osteochondroma
7	347	Epidermoid carcinoma	No tumor	No tumor
8	347	Mucoepidermoid carcinoma	No tumor	Osteochondroma
14	354	Epidermoid carcinoma	No tumor	No tumor
16, 17	359	Epidermoid carcinoma	Adenocarcinoma	No tumor
21	350	Epidermoid carcinoma	No tumor	No tumor
22	380	Epidermoid carcinoma	Adenocarcinoma	Osteochondroma
23	380	Epidermoid carcinoma	No tumor	No tumor
24	380	Epidermoid carcinoma	Mucus-producing adenocarcinoma (alveolar cell carcinoma?)	No tumor
25	380	Epidermoid carcinoma	No tumor	No tumor
26	380	Epidermoid carcinoma	Squamous cell carcinoma	No tumor

Keratinization was irregular and often parakeratosis was observed in the areas of the tumor in which the cells were loosely aggregated and undergoing an individual rather than a collective type of keratinization (Fig. 4). In dyskeratotic areas, a few epithelial cells tended to form pearls. The tumor seldom showed an undifferentiated growth with cellular pleomorphism and several mitotic figures (Fig. 5). A few tumors showed little nests of isolated pale cells (Figs. 6 and 7) of 3 types: mucin-producing cells (originating from the duct epithelium of sweat glands or salivary glands); squamous cells; and intermediate cells with minor tendencies towards differentiation.

Respiratory Tract. These tumors, although occurring rarely, were mainly adenocarcinomatous. Only in 1 rat did we observe an epidermoid tumor originating from the epithelium-covering cells. Sometimes, the tumors were seen in their early development and consisted predominantly of cubic or columnar cells arranged as regular or irregular tubular and papillary elements (Fig. 8) and supported by poorly developed fibrous stroma (Fig. 9).

In other cases, glandular structures were often imperfectly formed and appeared as sheet-like proliferations of undifferentiated or pleomorphic character. The cells showed a tendency to extend into the pulmonary parenchyma, thus simulating the microscopic features of the so-called alveolar cell carcinoma (Fig. 10). Sometimes, this was the prevailing pattern. The pulmonary air sacs were limited by 1 or more layers of cubic, columnar, or polyhedral cells with abundant cytoplasm that was faintly eosinophilic (Fig. 11), frequently, adenopapillary excrescences spreading into the alveolar spaces were present.

In some areas, foci of cellular polymorphism with hyperchromatic nuclei were noticed; mucin was produced in varying amounts and secreted into the lumen of the tubules and acini. There were small pools of mucin in which signet ring cells occurred, either alone or in small clusters (Fig. 12). The alveolar walls were often quite thick and, at times, showed an inflammatory infiltration.

As mentioned before, a single tumor showed squamous structures and appeared to have been formed mainly by spindle and oval undifferentiated cells (Fig. 12).

Bones. In the metacarpal and metatarsal regions of the 4 limbs, a large proliferation of cartilaginous tissues arose outward from the periosteum and, from the appearance of its cells, seemed to derive directly from the cortical bone (Fig. 14). The periosteum also grew and in some areas spread as finger-like prolongations into the newly formed cartilage (Fig. 15). In these places, a gradual transition between fibrous cartilage, periosteum, and bone could be noticed.

The newly formed cartilage appeared irregular with atypical areas; the cells, which had nuclei larger than the normal chondrocytes, lay in well-formed, capsulated lacunae. The cells occurred singly, in pairs, or in tetrads and, although of different size and shape, they usually contained a single, darkly stained nucleus. The cartilaginous growth was not homogeneous, as shown by the extension of the finger-like prolongations into the boundary of newly formed tissue. Besides the chondroblastic, chondrocytic, and angiomatous areas which indicated a rapid growth, there were also

cartilaginous zones possessing regressive features, such as fibrosis and hyalinosi. The perichondrium appeared often compressed and structurally altered fibrous tissue.

In some cases, the tumor growth was related to the stage of the endochondral ossification occurring below the "epiphyseal plate." Ossification was irregular, so that osseous trabeculae varied greatly in thickness and contours. In other cases, foci of active cellular proliferation, cartilaginous areas, chondrodevelopmental nests, and calcified bones occurred in deeper portions of the trabeculae (Fig. 18).

The new formation appeared to be an osteochondroma consisting essentially of a bony protuberance capped by cartilage and a fibrous layer, which represented the perichondrium.

The fibrous layer was continuous with the periosteum of the adjacent cortical bone and extended inward to form a separating and enclosing lobules of cartilage.

Control Animals. The control rats were kept under the same conditions as the experimental rats and at the appropriate times were subjected to a constant flow of air without vinyl chloride. None of these animals developed tumors or other parenchymal lesions developed by the rats that inhaled vinyl chloride. In a very few of the control rats, there was a swelling of the liver and kidneys.

DISCUSSION

As in many carcinogenesis studies in which multiple tumors arise in different tissues and organs, the data must be evaluated in terms of a more prompt positive response to be obtained with the ideal concentration of the carcinogenic compound. The cutaneous system is the most susceptible to the once effects of vinyl chloride.

Our experimental data do not explain why the cutaneous tumors developed in the same site, i.e., the region including the area in which the submaxillary and parotid glands are located. It is possible that the salivary glands may be involved in the concentration or excretion of vinyl chloride or some of its active decomposition products. This hypothesis is strongly supported by morphological findings showing the strong tendency of the developed tumor to appear as mucoepidermoid carcinoma, which indicates the contribution of the mucus glandular cells to the tumor growth. Such kinds of histotypes are often related to glandular aggregates, and, therefore, the histogenesis of mucoepidermoid carcinoma has been restricted to the branched intercalated ducts. This hypothetical interpretation is confirmed by future experiments in which the action of vinyl chloride should be restricted to the salivary system at the concentrations used, saturation and wetting of the skin might well be expected. Under these circumstances, the natural cleansing habit of the rat might add a self-cleaning problem with subsequent concentration of vinyl chloride in the salivary glands. The level of concentration could be the result of the difficulty of complete cleansing by the rat.

The neoplastic response of the lower respiratory tract, although of lesser magnitude, is of relevant interest, and

the tumors were morphologically similar to those described in the skin. The hypothesis that mucus-producing cells may be capable of retaining vinyl chloride or its decomposition products seems to be relevant once more. Obviously, a correct interpretation is required for the pathogenesis of the tumors and for their simultaneous incidence at the level of all 4 limbs.

REFERENCES

1. Banerjee, M., and Bates, R. Prevalence of Heteroploidy in Plastic Implant-Induced Primary Sarcomas. *Brit. J. Cancer*, 20: 555-563, 1966.
2. Brand, G., and Buoen, L. Polymer Tumorigenesis: Multiple Preneoplastic Clones in Priority Order with Clonal Inhibition. *Proc. Soc. Exptl. Biol. Med.*, 128: 1153-1157, 1968.
3. Brand, G., Buoen, L., and Brand, I. Malignant Transformation and Maturation in Non-dividing Cells during Polymer Tumorigenesis. *Proc. Soc. Exptl. Biol. Med.*, 174: 675-678, 1967.
4. Brand, G., Buoen, L., and Brand, I. Carcinogenesis from Polymer Implants: New Aspects from Chromosomal and Transplantation Studies during Premalignancy. *J. Natl. Cancer Inst.*, 39: 663-679, 1970.
5. Drostrey, H. Experimentelle Vorgänge zum Mechanismus der Carcinogenen Wirkung. *Arzneimittel-Forsch.*, 1: 383-395, 1951.
6. Hurper, W. C. Cancer Induction by Polyurethan and Polysilicone Plastics. *J. Natl. Cancer Inst.*, 33: 1005-1027, 1964.
7. Johnson, K., Buoen, L., Brand, I., and Brand, G. Polymer Tumorigenesis: Clonal Determination of Histopathological Characteristics during Early Preneoplasia: Relationships to Karyotype, Mouse Strain, and Sex. *J. Natl. Cancer Inst.*, 44: 785-793, 1970.
8. Kogan, A. Experimental Blastomogenesis Caused by Synthetic Polymers (Plastics). *Meditsina, Moscow*, 1: 215-237, 1965.
9. Mastromatteo, E., Fisher, A. M., Christi, H., and Danziger, D. Acute Inhalation Toxicity of Vinyl Chloride to Laboratory Animals. *Am. Ind. Hyg. Assoc. J.*, 21: 394-397, 1960.
10. Torkelson, T. R., Oyen, E., and Rowe, V. K. The Toxicity of Vinyl Chloride as Determined by Repeated Exposure of Laboratory Animals. *Ind. Hyg. J.*, 354-361, October 1961.
11. Van Duren, B. L., Sivak, A., Gohltschmidt, B. M., Katz, C., and Melchionne, S. Carcinogenicity of Halo-Ethers. *J. Natl. Cancer Inst.*, 43: 481-486, 1969.
12. Viola, P. L. Pathology of Vinyl Chloride. 16th International Congress of Occupational Health. (Communication No. 38), Tokyo, 1969.

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Figs. 1 to 18. All sections were stained with H & E.

Fig. 1. Squamous cell papilloma of the skin. X 25.

Fig. 2. Transitional stage from papilloma to infiltrative type of cancer. X 80.

Fig. 3. Finger-like trabeculae branch to form secondary processes showing horny pearl formation (arrows). X 25.

Fig. 4. Dyskeratotic area. Few epithelial cells with a tendency to form whorls. Little capacity to develop into horny pearls. X 250.

Fig. 5. Atypical cells partly lacking prickles and showing considerable variation in size, shape and many mitotic figures. X 250.

Fig. 6. Microepidermoid skin tumor. Occurrence of hydropic epidermoid cells, basal cells, columnar cells, and oxyphilic cells in various portions. X 100.

Fig. 7. Microepidermoid skin tumor, showing differentiation of masses of squamous epithelium from columnar cells, lining and proliferating into folded tubular spaces. X 100.

Fig. 8. Micronodular adenocarcinoma of the lung arising from a segmental bronchus. X 25.

Fig. 9. Detail of Fig. 8 showing tubular apertures made up by cells with hyperchromatic nuclei.

Fig. 10. Nodular bronchiolar alveolar mucus-secreting adenocarcinoma. X 100.

Fig. 11. Detail of Fig. 10, showing an alveologenic pattern. X 250.

Fig. 12. Mucus-producing cells with hyperchromatic and pleomorphic nuclei and occurrence of signet ring cells. X 250.

Fig. 13. Squamous cell carcinoma of the lung. X 100.

Fig. 14. Osteochondroma developing as a protuberance from the small bones of metacarpus and metatarsus. X 25.

Fig. 15. Magnification of Fig. 14. The protuberance consists of bone trabeculae, capped by cartilage, and a fibrous layer functioning as a capsule. X 100.

Fig. 16. Osteochondroma. Cartilaginous growth characterized by finger-like proliferation. X 100.

Fig. 17. Osteochondroma. Area of endochondral ossification. X 100.

Fig. 18. Cellular area of an osteochondroma showing the transition from cartilage to osteoid. X 100.

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