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B. Epidemiological Studies

MORTALITY EXPERIENCE OF A COHORT OF VINYL CHLORIDE-POLYVINYL CHLORIDE WORKERS*

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Since the publication on January 24th, in the *Wall Street Journal*, of three deaths from hemangiosarcoma of the liver in polyvinyl chloride (PVC) production workers at the B. F. Goodrich facility in Louisville, considerable data of scientific interest have been forthcoming. The data include the results of ongoing animal experimentation,¹ some clinical results on working populations,^{2,3} and reports of other cases or deaths from liver hemangiosarcoma in vinyl chloride-exposed workers.⁴ A remarkable amount has been accomplished in a short 3½-month period. However, to define fully the extent of the health problem associated with vinyl chloride (VC) exposure, it is clear that epidemiological approaches must be extended to include many individuals observed over sufficiently long periods of time to allow the full scope of any excess disease to be manifest.

While studies on the causes of death of exposed individuals offer the possibility of obtaining much more useful information, one must recognize the existence of several limitations. First, they are difficult and time-consuming to accomplish; one must trace and determine the status of *all* individuals having a defined exposure. This presents no difficulty for those workers still employed or retired and receiving company pensions. However, many individuals will have left the employ of a company prior to retirement and must be traced in order to obtain complete data. Second, sufficiently long follow-ups of exposed individuals must be completed. In other circumstances, it has been shown that occupationally induced cancers may take 20, 30, even 40 years before appearing in populations at risk. Thus, studies conducted over a short follow-up period may be misleading in that they are dominated by causes of death unrelated to the worker's exposures. Third, sufficiently large numbers of workers must be included in such studies to allow meaningful statistical considerations to be applied, particularly in causes of death that are found relatively frequently in the general population. Fourth, in such studies it is most desirable to have accurate information on vinyl chloride levels to which individuals in the cohort were exposed.

At this time, unfortunately, the relatively recent use of vinyl chloride does not allow us the luxury of having each, or even any, of the preceding four criteria satisfactorily fulfilled. Nevertheless, the urgency of the health problem resulting from past vinyl chloride exposures requires that all available preliminary data be scrutinized. Thus, an initial cohort study of vinyl chloride-polyvinyl chloride

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TABLE I
MAJOR WORK ACTIVITY OF 255 INDIVIDUALS DURING FIRST
10 YEARS OF VC EXPOSURE

Type of Work	No.
PVC production (reactor operation, reactor cleaning, PVC resin bagging)	151
Maintenance	60
Shipping	26
Laboratory	18
Total	255

workers was undertaken at a major production facility in western New York State.

By utilizing Union and Company records, a cohort of 257 individuals has been established, each of whom had been occupationally exposed to vinyl chloride for at least 5 years subsequent to 1946 in a polyvinyl chloride polymerization facility, having begun employment in the period 1946-1963.[†] This included all individuals so employed in this plant during this time. We have determined the mortality status of these individuals from the tenth anniversary of onset of exposure through April 1974. The 5-year exposure criterion was established for this preliminary study to establish the effects of significant exposures. The criterion that observations would begin only after 10 years from onset was selected so that one might focus on the long-term effects of vinyl chloride exposure. Although the exposures began in 1946, only a relatively few individuals were employed prior to 1951, when a significant increase in the work force took place. Thus, the majority of the cohort had a bare 20 years or less from onset of exposure.

The initial production facility consisted of six vinyl chloride monomer reaction vessels, a polymerization complex of four reactors, and a building for drying and bagging operations. From 1946 through 1950, seven men and one supervisor per shift handled the operations in all three areas. Thus, the production work force was approximately 30 men. In 1951, a significant expansion took place in the production facility; 16 additional polymerization reaction vessels and 12 monomer reactors were installed. The work force at this time expanded to approximately 150 hourly employees in the vinyl chloride and polyvinyl chloride operations. The only other significant change in this manufacturing complex came in 1960, when the production of vinyl chloride monomer ceased, due to the local unavailability of raw materials. From that point on, the vinyl chloride was received in tank cars from Texas. Little change occurred in the work force, however.

Of the 257 individuals exposed since 1946, 255 have been traced and their current health status established. Of the 255 so traced, work histories and, to a large extent, medical histories, have been documented. TABLE I shows a summary of their work activity during their first 10 years of employment in the PVC production facility. The majority of the 255 were employed directly in production. Typically, the first job of a newly hired individual would be the bagging of the

[†] We are grateful to the Goodyear Tire and Rubber Company and to Local 8-277 of the Oil, Chemical and Atomic Workers for their cooperation in providing this information.

725020

resin for shipment. During the course of this work, he would be periodically assigned to reactor cleaning or drying machine operation duty. Such cleaning operations were required weekly for each polymerization reactor and were routinely done without benefit of respiratory protection. As a man gained seniority he could be transferred to the reactor operations. In this job, he would be concerned with the operation and control of the polymerization process. On overtime, however, he might also be asked to engage in reactor cleaning operations. Additionally, whenever leaks or accidental releases of vinyl chloride occurred in the reactor area, the possibility of high exposures existed.

Nearly one-quarter of the individuals were employed predominantly in the maintenance department. Here, individuals would be assigned to correct mechanical problems anywhere in the plant. During times of mechanical breakdown in the reactor facility, their exposure to vinyl chloride could be significant. In general, however, this group would not experience extremely high exposures as often as those who would have engaged periodically in reactor cleaning. Parenthetically, one should note that a portion of the work experience of maintenance personnel may have been as production operators, but, in these cases, it would total less than 5 years.

A third group with lesser exposure was that of 26 men in the shipping department. Here, exposures were to gases that may evolve from the dried resin and from vinyl chloride released in other areas of the plant. A fourth group of 18 individuals, also with a lower exposure, was composed of laboratory personnel, testing the quality of both incoming chemicals and outgoing products. Because of the small number of individuals in the latter two groups, it was not practical to analyze separately their experience. They are thus included as part of a total cohort of individuals exposed to vinyl chloride in this one plant, although they may dilute somewhat the experiences of individuals with high exposures. We have excluded from consideration in this cohort individuals who were employed exclusively as plant guards or who worked outside the reactor and dryer buildings.

No data exist as to the levels to which these individuals may have been exposed in past years. Generally, measurements that were made prior to 1972 were to assure that the explosive limit of vinyl chloride was not exceeded in plant operations. As this limit exceeds 30,000 ppm, it has little relevance to current consideration of health effects.

In reviewing work practices and clinical symptoms experienced by individuals in the plant, it is clear that vinyl chloride concentrations could have been extremely high. Although reactors were purged at 20 in. of vacuum for up to 20 min prior to opening, a considerable amount of unreacted monomer could remain in the vessels. This was removed by insertion of an exhaust hose through the manhole cover to the bottom of the reactor vessel. The air pumped from the vessel was usually vented into the reactor room. The highest exposures occurred during cleaning when a man entered into the reactor to scrape the polyvinyl chloride resin from the walls and agitator, and unreacted monomer was released. Some data on the degree of exposure can be obtained from information provided by the current and past employees during physical examinations conducted in March 1974. Over 50% of a group of current and past employees experienced symptoms of dizziness, headache, or euphoria during work periods, and 14 out of 354 experienced concentrations sufficient to have caused loss of consciousness.⁹ Thus, peak exposures may often have exceeded 1,000 ppm and, during acute episodes, may have approached 10,000 ppm in the production facility.

TABLE 2 shows the age distribution of individuals in this cohort as they entered

725021

TABLE 2
AGE AT ENTRY INTO STUDY COHORT (AT 10 YEARS FROM
FIRST EMPLOYMENT)

Age	No.
25-29.9	42
30-34.9	64
35-39.9	60
40-44.9	29
45-49.9	32
50-54.9	15
55-59.9	9
60-64.9	2
65-69.9	2

TABLE 3
STATUS* OF 257 INDIVIDUALS EXPOSED TO VC FOR 5 OR MORE YEARS STARTING
BETWEEN 7/1/1946 AND 12/31/1963

	Examined and Interviewed	Interviewed	Deceased	Untraced	Total
Working at PVC produc- tion facility	139	10	—	—	149
Working elsewhere	18	43	—	—	61
Retired	13	8	—	—	21
Deceased	—	—	24	—	24
Untraced	—	—	—	2	2
Total	170	61	24	2	257

* Status recorded as of April 30, 1974.

the period of observation, that is, on the tenth anniversary of their employment in the production facility. As one can see, it was a relatively young group and one in which little disease and few deaths would be expected to occur. Over 50 percent of the men were under age 37 as they entered the cohort.

Information on the current status of the 257 individuals in the cohort is shown in TABLE 3. Over half are presently employed in the polyvinyl chloride production facility, although not all in areas with vinyl chloride exposure. Eighty-two individuals working elsewhere or retired were interviewed as to their current and past employment, current health, smoking habits, and alcoholic consumption. This was done to verify exposure history and obtain information required for future prospective observation. One hundred seventy individuals in the total group were examined. Twenty-four individuals were found to have died and 2 are as yet untraced.

TABLE 4 shows the expected and observed total mortality from cancer in

† Contact was made with individuals in Florida, California, Louisiana, Colorado, and many other states and Canada; all told, 24 of the 82 individuals traced were found alive in states other than New York. In accomplishing the tracing of over 99 percent of the cohort in less than 2 months, we owe an enormous debt to the members of the Oil, Chemical and Atomic Workers, Local 8-277, as all individuals were traced directly through personal information obtained from Union members. In particular, we would like to acknowledge the considerable time and effort put into this tracing by Mr. Ben Critelli, formerly of Local 8-277, and Mr. Frank Damon, of the Environmental Sciences Laboratory.

725022

different periods of time since first exposure to vinyl chloride for the group of 255 individuals traced for the study. Although observations are limited, the excess in total mortality and in deaths from cancer is unusual, considering the relatively short period of follow-up in this study. The specific causes of death are listed in TABLE 5. *Of the 24 deaths, 3 were due to hemangiosarcoma of the liver.* Each has been examined and characterized by Dr. Hans Popper and Dr. Louis B. Thomas of the National Cancer Institute* and is included among other tabulations of hemangiosarcoma presented at this conference.* Additionally, 1 death was due to bleeding esophageal varices consequent upon cirrhosis of the liver.

TABLE 4
EXPECTED* AND OBSERVED DEATHS FROM VARIOUS CAUSES AMONG 255 WORKERS
EXPOSED TO VC FOR 5 OR MORE YEARS STARTING BETWEEN 7/1/1946 AND 12/31/1963

Cause of Death	10-14.9 (1166)†		15-19.9 (784)		20-24.9 (374)		25-29.9 (69)		Total (2994)	
	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.
All Causes	6.1	10	6.6	7	5.0	7	1.3	0	19.0	24
All Cancer	1.2	3	1.4	3	1.1	3	0.3	0	3.9	9

* Expected deaths are based on mortality in New York State (other than New York City) in appropriate calendar years.

† Years since first exposure with person years at risk in parentheses.

TABLE 5
CAUSES OF DEATH AMONG 24 WORKERS EXPOSED TO VC FOR 5 OR MORE YEARS

Cancer of all sites	9
Hemangiosarcoma of liver	3
Neoplasms of lymphatic and hematopoietic tissues	2
Brain (glioblastoma)	1
Pancreas	1
Colon	1
Bone	1
Cirrhosis (with esophageal varices)	1
Postoperative bleeding (cholelithiasis)	1
Cardiovascular diseases	13

TABLE 6
WORK HISTORIES OF INDIVIDUALS DYING OF SELECTED CAUSES

Cause of Death	Date of Onset	Date of Death	Age at Death	Years of Latency	Years since First Exposure	Department
Hemangiosarcoma	10-46	03-70	60	23	23	PVC production
Hemangiosarcoma	10-47	08-61	41	14	14	PVC production
Hemangiosarcoma	06-51	05-68	54	17	17	PVC production
Bleeding esophageal varices	06-54	11-65	39	11	11	PVC production
Glioblastoma	11-52	04-68	63	12	15	Maintenance
Reticulum cell sarcoma	08-52	03-68	34	2	16	PVC production
Lymphosarcoma	05-58	04-70	32	12	12	Maintenance
						PVC production

Information solicited from relatives and fellow workers concerning the individual's drinking history indicate only very modest alcohol consumption and suggest that this case, too, may be causally related to the individual's exposure to vinyl chloride. Among the other cancers resulting in death were a glioblastoma, a lymphosarcoma, and a reticulum cell sarcoma. Our observation of a brain tumor and two lymphomas conforms to observations in other vinyl chloride-exposed populations⁷ and suggests the possibility that their origin may also be related to vinyl chloride exposures. In addition to the above, other malignancies were the underlying causes of death in this group of 24 workers.

The details of the work histories of the 3 workers who died of hemangiosarcoma and the other possible occupationally related cancers appear in TABLE 6. All but two worked extensively in the polymerization facility.

All of the hemangiosarcomas occurred in individuals who first worked prior to 1951. As the time from onset of exposure increases in cohort members with similar exposures, additional cases of occupational cancer may occur in this group of workers.

SUMMARY

These data are derived from early follow-up of individuals exposed for 5 or more years to vinyl chloride in a polymerization facility. At least 17 percent of the deaths that occurred were causally related to exposure to vinyl chloride. Longer periods of observation are required to provide information concerning the full spectrum of vinyl chloride-induced malignancies and their incidence among exposed workers.

These data speak for the need to prevent exposure to vinyl chloride and for surveillance and early disease detection of those who have experienced vinyl chloride exposures in the past.

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725024