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Mortality experience of styrene-polystyrene polymerization workers[1]

Initial findings

by WILLIAM J. NICHOLSON,[2] IRVING J. SELIKOFF[2] and HERBERT SEIDMAN[3]

NICHOLSON, W. J., SELIKOFF, I. J. and SEIDMAN, H. Mortality experience of styrene-polystyrene polymerization workers: Initial findings. *Scand. j. work environ. & health* 4 (1978): suppl. 2, 247—252. A group of 560 individuals has been identified as employed on 1 May 1960 with at least five years seniority in a plant manufacturing styrene and polystyrene. In this plant workplace exposures included styrene, benzene and ethylbenzene, among other materials. All of the 560 individuals have been traced through 1975 and their vital status determined. Expected and observed deaths, by cause, were determined from 1 May 1960 or the tenth anniversary of employment in the plant through 31 December 1975. Over this relatively short period of time a deficit of deaths compared to that of the general population was observed (106.41 expected versus 83 observed). Among the 83 deaths, one was of leukemia, one of lymphoma and an additional death was accompanied by leukemia. A review of 361 additional death certificates revealed five additional cases of leukemia and four of lymphoma. The available information from the limited follow-up in time of the cohort and from the randomly collected death certificates, while suggestive of a possible risk, is not definitive.

Key words: benzene, leukemia, lymphoma, mortality, polystyrene, styrene.

After the recognition in 1974 that exposure to vinyl chloride posed a significant human carcinogenic risk, producing liver hemangiosarcoma and the other malignant tumors (3, 5, 6), attention was directed to other widely used plastics in which monomer exposure to workers or the general population could be of significance. Among such monomers was styrene (vinyl benzene), widely used in the production of polystyrene, which has a chemical structure with similarities to that of vinyl chloride. Of additional concern was the possibility that worker exposure to benzene, a leukemogenic agent, could occur in the production and purification of styrene monomer. Furthermore, a potential for styrene exposure to the general population exists, albeit at considerably lower concentrations than those of the workplace. Such exposures could result from the leaching of unreacted styrene from food and beverage containers and from the combustion of polystyrene products. This latter source is of importance because polystyrene decomposes under heat to its monomer.

More recently, data have been presented that suggest styrene may be carcinogenic, producing leukemias and lymphomas (1, 4). This possibility follows the finding in 1976 of eight cases of leukemia in two styrene-butadiene production facilities in Texas, and a stated increase in deaths from

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leukemia and lymphoma in an Ohio styrene-butadiene rubber manufacturing plant. Of the eight cases six were among a group of 146 known deaths and two were under treatment or in remission.

For the investigation of whether health effects can be associated with styrene production and polymerization, a clinical survey and a mortality study of a large monomer and polymerization plant was conducted in 1975. The findings of the clinical survey appear elsewhere in these proceedings. Here we report the results of a mortality investigation of 560 long-term workmen employed at the facility.

MATERIALS AND METHODS

Among other information, a seniority list, as of 1 May 1960, was made available by Local 8—74 of the Oil Chemical and Atomic Workers' Union, which represented employees at the facility. The list was comprised of 711 individuals, 563 of whom had five years of employment in the plant. These latter were considered for inclusion in a cohort in which each individual would be followed prospectively from 1 May 1960 or upon attaining his 10th anniversary of employment. The five-year work criteria was applied so that the group would have significant exposure to styrene, and the 10-year criteria was applied so that long-term health effects, such as cancer, could also be considered. Of the 563 individuals, three were eliminated, one because he served as a union representative beginning in 1948 and was not working in the plant on 1 May 1960, one because of death prior to achieving his tenth anniversary of employment, and one, who was the sole female in the group, because different mortality statistics would be required.

Table 1. Distribution of ages and times of employment of 560 individuals at a styrene production and polymerization facility as of 1 May 1960.

Age (years)	Years since onset of work			
	5—9	10—14	15—19	All years
20—29	51	4		55
30—39	81	109	12	202
40—49	72	64	41	177
50—59	35	17	40	92
60—69	8	1	22	31
≥70		2	1	3
All ages	247	197	116	560

Table 2. Major work activity of 560 individuals during employment at a styrene production and polymerization facility.

Type of work	Number
High exposure categories	
Styrene production	56
Polystyrene polymerization and extrusion	129
Development and special products	53
Maintenance	206
Low exposure categories	
Service and utilities	116

Table 1 lists the breakdown according to seniority and age of the 560 individuals. Table 2 categorizes them according to major employment activities within the plant. The categorization of the departments according to relatively high or low exposure was made on the basis of air concentrations measured in a Health Hazard Evaluation during 1974 by the National Institute for Occupational Safety and Health (NIOSH), by worker descriptions, and by body burden of styrene metabolites measured during the course of the previously mentioned clinical survey. The air concentrations of styrene generally ranged from 5 to 20 ppm in the "high" exposure areas and less than 1 ppm in the "low" areas at the time of the NIOSH survey. However, wide excursions from these ranges occurred at specific locations. A good correlation of the presence of styrene metabolites with exposure classification is shown in the paper by Lorimer et al. (2) in these proceedings. Furthermore, while group exposures generally applied, there could be some individuals within each group who had a long-term exposure different from that of the group as a whole.

The current production operations are shown in fig. 1. Ethylbenzene is received at the plant in tank cars and reacted with superheated steam and a catalyst of iron

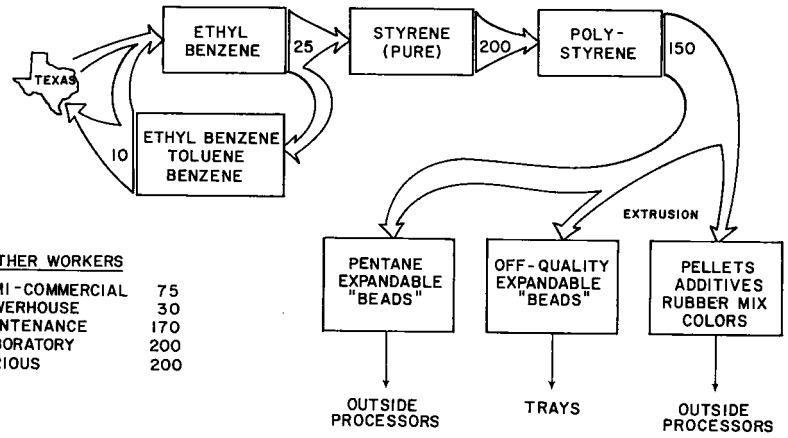

Fig. 1. Current operations and distribution of workmen in a styrene-polystyrene production facility.

oxide to produce styrene monomer. The crude styrene so produced is purified with the removal of unreacted ethylbenzene, benzene, toluene and xylene. These impurities are hydrogenated in another operation and distilled to separate the components for later use or distribution. Prior to 1963, benzene was produced at the plant from the by-products of coke ovens and reacted to form ethylbenzene.

In the polystyrene production, the purified styrene is reacted with water, catalysts, and various agents to produce polystyrene beads. These may later be impregnated with pentane in a closed system to form an expanded polymer. Alternatively, they may be extruded and formed into sheets. Other activities in the plant include the production of butadiene-styrene latex and pilot plant operations for research and development work on styrene polymers specific to a customer's specifications. A large maintenance force is employed at the plant and includes such trades as electricians, laborers, welders, insulators, and others. These men work throughout the plant as required, often at times of mechanical breakdown or leakage of various systems. Thus, exposure of individuals in this category could often be high. The utilities and service employees include those working in the power house and janitorial or other service jobs. Their exposures would be generally of a lower category.

RESULTS

All of the 560 individuals had been traced as of 31 December 1975, and their vital status determined. At that time, 233 were still employed at the facility, 83 were deceased, and 241 had retired or terminated employment. Each of this last group were contacted directly for verification as a member of the cohort and for information on work acitivities. For the 83 deceased, certificates of death were obtained in all cases. Additionally, when appropriate, clinical information, radiographs, and pathological specimens were sought from hospitals. Autopsy protocols were received for 18 cases and other information for 13.

Table 3. Expected and observed mortality experiences of 560 individuals employed at a styrene production and polymerization facility prior to 1 May 1955, followed 10 years after onset of exposure (1 May 1960 — 31 December 1975).

Cause of Death	Expected	Observed
All causes of death	106.41	83
Cancer	21.01	17
Cancer of the lung	6.99	6
Leukemia	0.79	1
Lymphomas	1.25	1
Other cancer	11.98	9
Heart and circulatory diseases	56.35	52
Respiratory diseases	6.64	1
Other causes of death	22.41	13

A review of these additional data revealed that one individual, listed as deceased from pancreatic cancer on the certificate of death, actually died from acute pancreatitis.

Table 3 shows the expected and observed mortality experience, as verified for the 560 individuals from 1 May 1960 through 31 December 1975. The expected rates of death were calculated with a modified life table analysis and data on the mortality experience of the general population of the United States. The results indicate that about 79 % as many deaths as expected occurred during this period of time. Deficits of this order are commonly found in studies comparing the mortality experience of working groups with that of the general population. This deficit results, in part, because groups of employed workmen are healthier than a corresponding age group in the general population which would include individuals terminally ill and others unable to hold jobs because of disability. This "healthy worker effect" can influence total mortality data for ten or more years and that of cancer for two to five years. While the data are limited because of small numbers, some information on these expected time effects can be seen in tables 4 and 5, where the cohort mortality experience in different calendar years indicates that death rates more closely approach those of the general population as time from identification of the cohort increases. This change is also seen in an analysis of mortality patterns according to time from first exposure where the highest ratios of observed to expected deaths are found in the groups having more than 20 years since first employment.

An analysis of mortality experience by extent of exposure is shown in table 6, where maintenance and production workers are compared to utility and service employees. No particular patterns were identified in this separate mortality analysis, but again the data were limited by small numbers.

Because of the high exposure to benzene experienced by some individuals in the cohort during the 1943—1962 period of time, and to a lesser extent thereafter, special attention was paid to leukemia as

Table 4. Expected and observed mortality experiences of 560 styrene production and polymerization workmen in three calendar periods of time.

Cause of death	1960—1965		1966—1970		1971—1975	
	Expected	Observed	Expected	Observed	Expected	Observed
All causes of death	26.76	14	35.68	28	43.97	41
Cancer	4.78	2	6.87	6	9.36	9
Heart and circulatory diseases	14.01	8	18.42	18	23.92	26
Respiratory diseases	1.54	0	2.25	0	2.85	1
Other	6.43	4	8.14	4	7.84	5

Table 5. Expected and observed mortality experiences of 560 styrene production and polymerization workmen according to years from onset of employment.

Cause of death	10—19		20—29		≥30	
	Expected	Observed	Expected	Observed	Expected	Observed
All causes of death	39.78	20	59.84	59	6.79	4
Cancer	7.25	2	12.33	15	1.43	0
Heart and circulatory diseases	20.06	11	32.34	37	3.95	4
Respiratory diseases	2.30	0	3.84	1	0.50	0
Other	10.17	7	11.33	6	0.91	0

Table 6. Expected and observed mortality experiences of 560 styrene production and polymerization workmen according to work activity.

Cause of death	Production and polymerization		Maintenance		Utilities service	
	Expected	Observed	Expected	Observed	Expected	Observed
All causes of death	40.26	31	42.49	36	23.66	16
Cancer	8.17	4	8.05	10	4.79	3
Heart and circulatory diseases	20.56	20	23.22	23	12.57	9
Respiratory diseases	2.41	0	2.74	0	1.49	1
Other	9.12	7	8.48	3	4.81	3

a cause of death. While one death in the cohort was directly attributed to leukemia, a second individual, deceased of a coronary, also had leukemia at the time of death. During the course of this study, an additional 21 death certificates of individuals who died in recent years were made available to us from union files. These were of individuals that did not have five years of employment as of 1960 and were thus not included in the cohort under consideration. Among these 21 deaths, there was an additional leukemia and an additional lymphoma. Thus, in 104 deaths, there were two of leukemia, one with leukemia and two lymphomas. While the total number is small, the finding of five leukemias and lymphomas among 104 deaths suggested that further investigations of the plant mortality experience would be useful. This information was provided to the company and the union representing the plant workers. Following its receipt, the company initiated an epidemiologic study of all individuals employed for six months or more at that particular plant and supplied information on its progress to NIOSH. From information on 444 death certificates it was determined that seven deaths involved leukemia and an additional five, diseases of the lymph system. The work histories and exposures of the 444 individuals, however, were not available. The breakdown was as follows:

Acute lymphoblastic leukemia	1
Acute blastic leukemia	1
Acute myelogenous leukemia	3
Chronic lymphatic leukemia	1
Chronic myelogenous leukemia	1
Hodgkins disease	3
Lymphosarcoma	1
Retroperitoneal lymphoma	1

Unfortunately, the small numbers and limited follow-up in time of the cohort does not provide definitive information on the risk of death from leukemia or lymphoma in this plant (other than to indicate that it was not extraordinary). Similarly, available information from the randomly collected death certificates, while suggestive of an excess risk, is not definitive. More extensive epidemiologic studies, over longer time periods, will be required. Such studies, however, must take into account the possible exposures to benzene in the consideration of the etiology of leukemia.

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QUESTIONS AND ANSWERS

Question to: Dr. ALF FISCHBEIN

Dr. RANTANEN: We can expect that styrene is a weak carcinogen. Your exposure time was about 20—25 years and latency time maximally 20—25 years. Could we expect that we now are registering only latency period and 10 to 20 years more are needed to show excess malignancy frequencies?

Dr. FISCHBEIN: The period of clinical latency is an important consideration in the evaluation of environmentally induced malignant disease. For certain asbestos related tumors, pleural and peritoneal mesothelioma, for example, the latency period may be very long and the tumors usually do not become clinically manifest until 30—40 years after onset of exposure. The mortality study presented did not give any conclusive evidence because of the relatively young population and short latency period. Conclusive information is urgently needed, however, in order to protect those currently exposed. Methodological approaches other than mortality studies may also contribute to the speedy solution of this problem.

Interaction and synergism between styrene and other chemicals in the work environment should also be taken into account. Both carcinogenic potential and latency period may be affected by such factors.

Comments on the statement of Dr. Rantanen in which he to placed styrene as a weak carcinogen.

Prof. THIESS: From my point of view there isn't any evidence that allows us to call styrene a weak carcinogen at this moment. We have experiences since 1931; that means *46 years*. We should avoid that unskilled people will take any action due to this remark of Dr. Rantanen. Our duty is to inform people but not to raise fears.

Dr. HILDEBRAND: I would like to put the remark of Dr. Rantanen into the correct perspective. You only could assume styrene to be a weak carcinogen, but up to now there is no experimental evidence for that. This is based on three other major studies which are now complete (NCJ, MCA, MALTONI) and the results, though not all conclusive, do not show any clear evidence for styrene to be a clearcut carcinogen, not even a weak one.