

OCCUPATIONAL HAZARDS IN PRODUCTION AND PROCESSING OF STYRENE POLYMERS - EPIDEMIOLOGIC FINDINGS

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INTRODUCTION

Of the major plastic monomers, styrene is exceeded only by ethylene, propylene and vinyl chloride in terms of production. In 1977, approximately 3×10^6 metric tons were produced in the United States and 7×10^6 metric tons worldwide (IARC, 1979). Approximately 60% of the monomer produced was used in homopolymers, largely for the packaging industry. Other important uses of styrene are in the production of copolymers with acrylonitrile (SAN) and acrylonitrile and butadiene (ABS). Styrene also finds widespread use as a copolymer with butadiene in the production of the synthetic elastomer, styrene-butadiene rubber (SBR), which forms the basis of approximately 80% of U.S. rubber products. Finally, it is extensively used as a solvent and cross-linking agent for polyester resins in the fiber reinforced plastic (FRP) industry. Estimates of the number of workers employed in the various industries using styrene-based polymers are given in Table 1 along with typical exposure levels (Tossavainen, 1978). In addition to occupational exposure, low-level environmental contamination can occur from combustion of styrene-based products, as the thermal decomposition of polystyrene leads to evolution of the monomer, in contrast to other polymer materials.

MORTALITY STUDIES OF STYRENE-EXPOSED WORKERS

Studies on the mortality of populations exposed to styrene are fraught with difficulty because of confound-

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Table 1
Occupational exposures to styrene

Process	Percent of styrene production	Number of workers involved	Typical exposure (ppm)
Monomer production	100	10,000	1 - 20
Polymer production (PS,ABS,SBR)	60 - 70	50,000	1 - 20
Reinforced plastics production (FRP)	20 - 30	200,000	20 - 300
Polymer processing (PS,ABS,SBR)	5 - 10	1,000,000	0.01 - 1

From Tossavainen, 1978

ing exposures to other known carcinogenic materials. Benzene exposures can occur in the production of styrene monomer, as the principal production process utilizes benzene to produce ethylbenzene, which, in turn, is dehydrogenated to form styrene. Copolymerization involves exposures to acrylonitrile and/or butadiene, which are carcinogenic in animals (Huff, 1983). Finally, some of the additives used in styrene products may be carcinogenic, as well as other chemicals used in facilities producing styrene or polystyrene.

Only three studies provide data on possible human carcinogenicity of styrene, each having some of the confounding exposures mentioned above. All were of groups of individuals employed in monomer production, polymerization or polymer fabrication, where exposures were relatively limited. No data exist on the mortality of individuals employed in the FRP industry, where styrene concentrations were (and are) commonly ten times higher. Table 2 lists the cohorts observed and some of the characteristics of the three studies.

As can be seen from Table 2, the large number of individuals lost to follow-up in the study by Frentzel-Beyme et al (1978) severely limits its usefulness. Of those exposed, 7% of the German workers and 71% of foreign "guest workers" were untraced. Of those traced, 74 had died, 12 from cancer. Only 37 deaths occurred in those with five or more years of exposure. The overall result did not demonstrate excess mortality for any cause of death. However, the limitations of the study are clear.

Table 2
Population and follow-up characteristics of
three studies of styrene exposed workers

Study	Country	Analysis cohort size	Percent traced	Number of deaths analyzed	Percent of total
Ott et al. 1980	USA	2904	97.4	303	10.4
Nicholson et al. 1978	USA	560	100.0	83	14.8
Frentzel-Beyme et al. 1978	GER	1960	93.0Ger 29.0For	73	3.7

	Minimum exposure (years)	Minimum latency (years)	Years follow-up	Exposures
Ott et al. 1980	1	1	1940-1975	<10 ppm (3) ^a
Nicholson et al. 1978	5	10	1960-1975	<20 ppm (5)
Frentzel-Beyme et al. 1978	1 mo.	1 mo.	1956-1976	< 1 ppm ^b

^a () = Estimated average exposure

^b Current measurement after installation of controls

The study of Nicholson et al (1978) successfully traced all of 563 men employed in styrene production, polymerization and polymer processing who had 5 years of employment on May 1, 1960 and were 10 years from onset of work in a large U.S. production facility. The basic mortality data are shown in Table 3 and demonstrate no excess mortality from any cause of death. Analyses according to years from onset of exposure and calendar years of observation did not reveal any pattern of excess mortality. However, because of the limited number of deaths, the data can be used only to establish upper limits of risk. For example, the data are only sufficient to indicate that the SMR for lymphoma or leukemia is less than 280 at the 0.05 level of significance and that of lung cancer, less than 220. While no excess mortality was identified in the cohort observed, the above publication mentioned the existence of 7 deaths from leukemia and 5 of malignancy of the lymphatic system among 444 deaths known to have occurred in the plant workforce. While the ages of death were not available for exact proportionate mortality calculations, the number of lymphomas is in line with expectations, while leukemia appears to be in excess by as much as a factor of two. However, the possibility of high exposures to benzene in the facility during earlier years weakens the likelihood

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Table 3

Expected and observed mortality experiences of
560 individuals employed in styrene production
and polymerization prior to 1 May 1955, followed
ten years after onset of exposure
(1 May 1960 — 31 December 1975)

Cause of Death	Expected	Observed	SMR
All causes	106.41	83	78
Cancer	21.01	17	81
Cancer of the lung	6.99	6	117
Leukemia	0.79	1	126
Lymphomas	1.25	1	80
Other cancer	11.98	9	75
Heart and circulatory dis.	56.35	52	92
Respiratory diseases	6.64	1	15
Other causes of death	22.41	13	58

From Nicholson et al. 1978

of association of any possible excess of leukemia with styrene exposure.

The final study of styrene mortality is that of Ott et al (1980) who described the experience of 2,904 individuals with potential exposure to styrene prior to January 1, 1976. Three hundred three deaths occurred, 292 among production and nonprofessional research employees. The mortality experience for this latter group is shown in Table 4 and is compared to the expected deaths calculated from U.S. white male rates and rates from observations on other company employees. As can be seen, the mortality of styrene-exposed individuals compares favorably with each group; the only excess of note being six leukemias compared to 2.9 expected using U.S. rates and 1.6 from company rates. Lymphomas were also elevated, but not at an 0.05 level of significance. The excess leukemia was further investigated in an analysis of cancer incidence in the styrene-exposed population compared to that expected from rates of the Third National Cancer Survey. In this analysis, it was found that a significant number of lymphatic leukemias (5 observed vs. 0.26 expected) occurred in individuals who were exposed to styrene (< 5 ppm), ethylbenzene (< 5 ppm), polystyrene extrusion fumes, and colorants. Indeed, four of the five cases worked in the same general area during the period of time, 1947-1948, although their dates of death and other exposures varied widely. Interestingly, there were no deaths of lymphocytic leukemia among 442 individuals exposed to higher

Table 4

Observed and expected deaths by cause for total production
and non-professional research employees (2310 men), 1940-1976

Causes	Observed deaths	Expected deaths US white males	SMR	Expected deaths, Company comparison	SMR
All causes	282	357.8	79	287.6	98
Malignant neoplasms	55	64.2	87	65.0	85
Respiratory system	14	20.8	67	23.9	59
Digestive system	16	18.0	89	21.2	67
Lymphatic and hematopoietic system except leukemia	6	4.5	133	2.6	230
Leukemia	6	2.9	207	1.6	375
Other sites	13	18.0	72	15.7	83
Cardiovascular disease	143	172.4	83	141.5	101
Nonmalignant respiratory dis.	12	14.3	84	10.0	120
All other causes	72	106.9	67	71.1	101

From Ott et al. 1980

concentrations of styrene (5-9 ppm). Because of a lack of a definitive exposure-response-relationship and the presence of possible confounding exposures, the authors refrained from drawing any conclusions on an etiological relationship.

In 1976, nine cases of various types of leukemia were identified in two SBR plants and reported to the U.S. National Institute for Occupational Safety and Health (Meinhardt et al, 1978). All occurred after 1971 in a population of 5,600 workers. No data were presented on the expected numbers of deaths from leukemia in the group. Concern generated by the findings in the two plants led to reports on the leukemias present in two large ongoing studies of rubber workers. McMichael et al (1976) reported a relative risk of 6.2 for lymphatic and hematopoietic malignancies among employees producing elastomers, including SBR. However, this was based upon only 6 cases, 3 leukemias and 3 lymphomas. In a subsequent case control study of the same plant, a relative risk of 2.4 was found for the same exposure group (Spirtas et al, 1976). The difference in the two values reflect the uncertainties associated with small numbers of cases. A similar investigation by Monson et al (1978) showed an excess of leukemia to be present in calendering, extrusion, tire building and rubberized fabrics. However, the excess was associated with exposure to solvents and not to styrene.

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Since 1976, considerable interest has existed in potential carcinogenicity of styrene. This has been heightened by the data on mutagenicity and possible carcinogenicity of styrene and styrene oxide (Huff, 1983). Some suggestive human data are available from studies of polymerization workers and SBR production facilities. The irony of the situation is that no studies have been conducted of groups exposed to the enormously higher concentrations found in the FRP industry. The data available on styrene carcinogenicity are such that they can provide no assurance of safety at these higher exposures.

CARCINOGENIC RISK FROM COMONOMERS USED WITH STYRENE

The two principal comonomers used in styrene-based copolymers have each been shown to be carcinogenic in animals. Of these, acrylonitrile has also been associated with lung cancer in humans. In a group of 1,345 male employees, with potential exposure to acrylonitrile and followed from 1956 through 1976, 8 cases of lung cancer occurred compared with 4.4 expected from company rates (O'Berg, 1980). Further, there was a correlation of increased risk with intensity and duration of exposure. Among production workers employed between 1950 and 1952, 6 lung cancer deaths were observed vs. 1.5 expected ($p < 0.01$). A second study of 327 employees of a rubber chemicals plant with potential exposure to acrylonitrile identified 9 deaths of lung cancer compared to 5.9 expected, based on mortality rates for U.S. white males (4.7 based on mortality rates for other rubber workers from the same city) (Delzell and Monson, 1982). The excess was greatest among those who had worked for more than 5 years in the facility. These data, while limited by the small numbers, strongly suggest that acrylonitrile is carcinogenic for humans.

While butadiene has been demonstrably carcinogenic in animals (Huff, 1983), no data are available from human exposures.

CLINICAL FINDINGS AMONG STYRENE-EXPOSED WORKERS

A variety of symptoms have been reported from styrene exposure, dating from the rapid increase in production during World War II. Eye, nose and throat irritation,

various respiratory symptoms, and gastrointestinal disturbances, such as nausea, vomiting and loss of appetite, are commonly reported by styrene-exposed workers. Other abnormalities reported include headaches, tiredness and sleep disturbance. After a period of exposure, adaptation may occur and there can be a decrease in the various symptoms. Nevertheless, significant alterations still exist among currently employed workers.

Several systematic studies of the various clinical effects from styrene exposure have been conducted in recent years. Many of these focused on possible neurological alterations and clearly demonstrated adverse findings at moderate styrene exposures (less than most national standards). The most extensive of these is that by investigators from the Institute of Occupational Health of Finland (Seppäläinen and Härkönen, 1976; Lindström et al, 1976; Härkönen, 1977; Härkönen et al, 1978). They examined 98 workers employed at 24 plants manufacturing FRP products. Air concentrations were sampled and ranged from 5 to 300 ppm. The means of five post-workday urine mandalic acid (MA) concentrations ranged from 7 to 4,700 mg/l with a linear relationship existing between the log of the MA concentration and the log of the styrene concentration. The mean value of MA in the population was 808 mg/l and corresponded to an exposure of about 40 ppm of styrene. Abnormal EEG's were found in 30% of those with MA in excess of 700 mg/l, compared to about 10% for those with lower MA values and normal controls (Seppäläinen and Härkönen, 1976). Lindström et al (1976) noted increased visuomotor inaccuracy (symmetry drawing and Bourdon-Wiersma tests) and lowered psychomotor performance (Mira test) for various MA concentrations ranging from 800-2,000 mg/l (See also: Härkönen et al, 1978). Fatigue, irritation, difficulty in concentration, nausea, dizziness, and lightheadedness were more frequently reported by the styrene-exposed workers than by unexposed controls (Härkönen, 1977).

A deteriorating EEG among styrene workers has also been described by Klimkova-Deutschova et al (1973). Alterations of nerve conduction have been documented by Rosén et al (1978) who observed an increased duration and decreased amplitude of sensory action potentials. Lilis et al (1978) suggested the possibility of a decrease in peroneal nerve conduction velocity. The decrease, however, was only associated with length of employment and not intensity of expo-

sure. Subjective symptoms of physical and mental tiredness after styrene exposure have been reported by Klimkova-Deut-schova et al (1973) and Cherry et al (1980), among others. The reported neurological findings among styrene-exposed workers are less serious than those reported in some other groups occupationally exposed to solvents, such as as painters (Lindström, 1980; Hane et al, 1977). However, the continued exposure to concentrations causing the observed abnormalities may lead to more serious central nervous system impairment.

In addition to neurological disturbances, alterations of pulmonary function have been noted among styrene-exposed workers. Lorimer et al (1977), in an examination of 494 polymerization workers, found a reduction in FEV₁ to be associated with intensity of exposure and with urine MA concentration. Further, the workers in the higher exposed group reported a greater percentage of acute and recurrent lower respiratory symptoms. Härkönen (1977) reported an increase in incidence of chronic bronchitis which correlated with intensity of exposure. On the other hand, Axelson et al (1978) did not find any abnormalities of pulmonary function among 27 FRP boat manufacturing workers.

Laboratory test results have been rather unremarkable. Lorimer et al (1977) suggested the possibility of increased lymphocytosis among polymerization workers and Checkoway (1982) found a correlation between decreased red blood cell count and increased basophil count with styrene/ butadiene exposure. Increased blood enzyme concentrations, characteristic of abnormal liver function, occasionally have been reported. Lorimer et al (1977) found a significant increase in concentrations of GGTP (gamma glutamyl transpeptidase) and Hotz (1980), noted increased concentrations of OCT (orinithine carbamoyl transferase) and ALAT (alanine amino transferase) among polymerization workers.

SUMMARY OF HUMAN MORTALITY AND MORBIDITY

The limited epidemiological studies of mortality associated with styrene exposure do not demonstrate any excess cancer risk that can be attributed to styrene, although elevated risks for leukemia have been noted in exposed groups. However, these excesses may be related to exposures

to other chemicals, such as benzene. The studies are severely limited because of the relatively low styrene exposure of the groups studied. They provide no guidance on carcinogenic risk in populations much more heavily exposed as in the FRP industry. The significant clinical findings among styrene-exposed workers are largely limited to abnormalities of the central nervous system, where a variety of objective and subjective symptoms have been reported in the FRP industry. Concern for long-term degenerative neurological disease exists for continued long-term exposure in this industry. The possibility of pulmonary effects from styrene exposure has also been noted.

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