

Epidemiologic investigations of styrene-butadiene rubber production and reinforced plastics production

by THEODORE J. MEINHARDT, RONALD J. YOUNG
and RICHARD W. HARTLE¹

MEINHARDT, T. J., YOUNG, R. J. and HARTLE, R. W. Epidemiologic investigations of styrene-butadiene rubber production and reinforced plastics production. *Scand. j. work environ. & health* 4 (1978): suppl. 2, 240—246. The United States National Institute for Occupational Safety and Health (NIOSH) began an epidemiologic study of workers employed in the styrene-butadiene rubber (SBR) industry during 1976. This study was prompted by reports of relatively high numbers of leukemia deaths occurring within SBR production work populations. Simultaneous with the initiation of this investigation, the University of North Carolina released a report associating an excess risk of death due to hematopoietic and lymphatic malignancies among workers producing several synthetic rubbers, including SBR. This report presents NIOSH's preliminary mortality observations and a discussion of progress made on the analyses of contaminants found in two SBR production facilities. Currently, NIOSH is determining the feasibility of doing an epidemiologic study in the reinforced plastics industry. Interest in this study developed as part of an effort to determine health hazards associated with occupational exposure to styrene. Most of the technology for the reinforced plastics industry developed in the 1950s, and therefore this process represents a relatively new industry. This report also includes information on environmental conditions observed in the reinforced plastics industry and enumerates some of the complicating characteristics of this industry which increase the complexity of this study.

The only epidemiologic studies of which I am aware that have considered the mortality patterns of workers exposed to styrene are the two studies being presented today by Dr. Thiess and Dr. Fischbein. These reports are concerned with the mortality patterns of individuals who have worked in industries that involve environmental exposure to low levels of

styrene. My presentation outlines ongoing research efforts being made by the National Institute for Occupational Safety and Health (NIOSH) in United States industries with both low and high level environmental exposures to styrene. Unfortunately, these efforts have not as yet progressed to the point where analyses and results are available.

Potential harmful effects associated with exposure to styrene have been noted in the literature for years. It was not until leukemia cases were reported in styrene-butadiene rubber (SBR) plants in

¹ National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluations and Field Studies, Industry-Wide Studies Branch, Robert A. Taft Laboratories, Cincinnati, Ohio, U.S.A.

the United States in March of 1976 that NIOSH focused its attention on the possible carcinogenicity of styrene. Almost simultaneously with NIOSH's decision in 1976 to study the SBR industry, a number of articles appeared concerning the possible mutagenicity and carcinogenicity of styrene and its metabolites.

Styrene is known to be metabolized to styrene oxide (2), which was shown by several authors to be mutagenic in the Ames microbial test system (5, 10). Finnish researchers reported that an unidentified styrene metabolite was positive for microbial mutagenesis after activation of styrene by liver microsomes (16). The mutagenesis of a styrene metabolite indicates that styrene exposure may be related to carcinogenesis since 90 % of the carcinogens, identified through various animal test systems, studied by the Ames tests have been shown to be mutagenic (6).

The eight malignancies of the hematopoietic and lymphatic systems among SBR workers were of particular concern in view of a previous study reporting a "statistically reliable" decrease in the amounts of blood hemoglobin, erythrocytes and thrombocytes in rubber processing plant workers (1). Additionally, a separate preliminary epidemiologic study of workers exposed primarily to styrene discussed what appeared to be an excessive percentage of deaths due to leukemia and lymphomas. This latter finding must be tested further because the deaths were identified from a worker population with potential concomitant exposure to benzene and other recognized chemical hazards (4).

The possibility that exposure to styrene may be associated with leukemia and other forms of cancer could represent a serious occupational health problem. In the United States alone, it is estimated that 4,082,400 t of styrene were produced in 1977 with an estimated 500,000 workers occupationally exposed to this substance. Thus, NIOSH decided to pursue further the question of human carcinogenicity of styrene by studying employees in the reinforced plastics industry where there is much greater potential for styrene exposure than in the SBR industry and not nearly as many confounding chemicals.

EPIDEMIOLOGIC INVESTIGATION IN THE STYRENE-BUTADIENE RUBBER INDUSTRY

Styrene-butadiene rubber (SBR) is the most widely used synthetic rubber in the world. The United States Government foresaw shortages of natural rubber during World War II and financed construction of fifteen SBR plants, sixteen butadiene production facilities and five styrene plants. Between 1946 and 1955, these plants were sold to various private companies (12).

In January 1976 two men employed at adjacent SBR facilities in Port Neches, Texas, died of leukemia. This information, combined with knowledge of other leukemia cases at the two SBR plants, began to concern the local Oil, Chemical and Atomic Workers' Union representatives, who in turn relayed this concern to the company. Consequently, local company officials reviewed plant records and identified eight leukemia cases among employees within the past few years. This apparent excess prompted the company officials to request that NIOSH investigate the possibility of an association between employment in SBR production and the development of leukemia or related malignancies.

Simultaneous with NIOSH becoming aware of leukemia cases among workers at SBR facilities, McMichael et al. (7) from the University of North Carolina's Occupational Health Studies Group reported the cause specific mortality experience among a cohort of 6,678 male rubber and tire manufacturing workers and various subgroups of that total population (broken down by occupational job titles). A relative risk for lymphatic and hematopoietic malignancies of 6.2 was reported for a synthetic plant, a work area that included production of elastomers, particularly SBR. In a subsequent unpublished report (entitled "Toxicologic, Industrial Hygiene and Epidemiologic Considerations in the Possible Association Between SBR Manufacturing and Neoplasms of Lymphatic and Hematopoietic Tissues") by McMichael et al. the relative risk for hematopoietic and lymphatic systems was reduced to 2.4 based on a case-

Table 1. Observed leukemia initially reported among currently employed, retired or pensioned SBR workers.

Case	Duration of employment	Beginning date of employment (year)	Date of death (year)	Age at death	Cell type ^a
1	19	1950	1971	62	Lymphocytic leukemia
2	20	1955	1976	46	Acute myelogenous leukemia
3	21	1958	Alive	—	Lymphocytic leukemia
4	25	1951	1976	59	Acute myelocytic leukemia
5	17	1943	1972	77	Acute lymphoblastic leukemia
6	28	1943	1971	64	Myelocytic leukemia
7	25	—	1978	52	Acute myelocytic leukemia
8	23	1943	1967	65	Acute myeloblastic leukemia
9	22	1943	Alive	—	Chronic lymphatic leukemia

^a Diagnosis based on company record.

Table 2. A typical SBR recipe (part per 100 parts monomer).

Ingredient	Quantity
Butadiene	75.0
Styrene	25.0
n-Dodecyl mercaptan	0.5
Paramenthane hydroperoxide	0.10
Sodium formaldehyde sulfoxylate	0.10
Soap flakes	5.0
Water	180.0

control study at the same plant, but was still statistically significant.

In addition to the eight leukemia cases initially identified by the companies, another case was identified by NIOSH shortly after it initiated the study. Table 1 presents basic information on these individuals, as well as their specific cell type of leukemia. It is important to remember that these initially observed diagnoses are based on company records and that some of these may be assigned different International Classification of Disease Codes when all of the information on the death certificates is considered. Additionally, it is known that case number five was treated for recurring respiratory infections with a drug which has been linked with blood dyscrasia and that case number nine had potential short-term exposure to

benzene while he worked on an experimental project. Eight of these nine cases were diagnosed after 1971. These cases were identified from company health records which were available only on active, retired, or pensioned employees. Therefore, the health status of terminated employees, the largest segment of people who have worked at the plants, remains to be evaluated.

The two SBR plants in Port Neches, Texas, were selected for study so that the potential of a health risk in these two plants could be evaluated and the salient question of potential health hazards associated with SBR production could be addressed. The method of study chosen for this investigation was a retrospective cohort mortality design. The population, composed of approximately 5,600 workers, represents a large stable work force for which adequate personnel records are available. Later this year data collection on all members of the study population should be complete, and analysis can begin.

Process and chemical hazards

Styrene-butadiene rubber is a copolymer of styrene and butadiene. It is made through an emulsion polymerization process. An emulsion system normally con-

tains water, monomers, initiator, and foam (12). An initiator system which usually contains paramenthane hydroperoxide and sodium formaldehyde sulfoxylate is used in combination with a mercaptan to polymerize butadiene and styrene. A typical SBR recipe is found in table 2. The styrene butadiene, soap, and initiator are pumped continuously from separate storage tanks into and through a series of agitated reactors maintained at proper conditions such that the required degree of conversion is reached at the exit of the last reactor (12). The termination of the reaction is caused by addition of a "shortstop" such as sodium dimethyldithiocarbamate or sodium polysulfide. The "shortstop" reacts rapidly with free radicals and oxidizing agents and thus destroys any remaining initiator and prevents the formation of new chains. The unreacted monomers are recovered, first the butadiene by distillation and then the styrene by steam stripping. An antioxidant, such as a mixed alkylated diphenylamine, is added to protect the product from oxidation. The latex is partially coagulated with brine and then fully coagulated with dilute sulfuric acid. The coagulated crumb is then washed, dried, and baled for shipment (12).

Representative employee 8-h time-weighted average exposures to styrene and butadiene for specific job classifications in one of the SBR facilities are depicted in table 3. The United States threshold limit values for exposure to

styrene and butadiene are 100 ppm and 1,000 ppm, respectively. It is readily seen that exposures to both chemicals are low when compared with existing United States standards.

Other chemicals used in SBR production have also been associated with a carcinogenic risk. Phenyl-beta-naphthylamine was historically used as an antioxidant at some SBR facilities. This chemical has been demonstrated to be metabolized in the body to beta-naphthylamine, a known human bladder carcinogen. Another example is the extender oils used in approximately 70 % of SBR production (11, 13). Furthermore the Oil, Chemical, and Atomic Workers' Union arranged for Kettering Laboratories to conduct skin painting experiments with five extender oils used at one of the SBR facilities in the United States. Preliminary results indicated a positive carcinogenic response for three of these oils in the animal test system (3). Of the recognized potential chemical hazards used in the SBR industry, only styrene has been speculatively linked with a possible risk of hematopoietic and lymphatic malignancies. However, it would be inappropriate at the present time to attribute the observed leukemia cases solely to the occupational exposure of styrene because of the complex chemical nature of this industry and the presence of other chemicals which have also been associated with cancer.

Table 3. SBR — Summary plant data of employees' 8-h time-weighted average (TWA) exposure to styrene and butadiene at an SBR facility, April 1977.

Job classification	No. of samples	Styrene				Butadiene			
		Range (ppm) (high-low)	Mean (ppm)	Median (ppm)	TWA	Range (ppm) (high-low)	Mean (ppm)	Median (ppm)	TWA
Technical services personnel	12	2.14—0.09	0.55	0.37	0.55	114.55—0.21	19.85	0.63	19.68
Production foreman	1	0.15—0.15	0.15	0.15	0.15	1.16—1.16	1.16	1.16	1.16
Head production operator	5	0.55—0.11	0.28	0.14	0.27	69.61—0.25	15.50	0.27	15.61
Production operator	24	2.14—0.12	0.38	0.16	0.39	33.21—0.23	3.30	0.30	3.41
Operator helper	3	0.16—0.14	0.15	0.15	0.15	1.81—0.26	0.79	0.30	0.77
Pipefitter	8	0.22—0.09	0.13	0.10	0.13	1.78—0.18	0.74	0.41	0.73
Electrician	5	0.13—0.09	0.11	0.10	0.11	0.34—0.18	0.22	0.20	0.22
Maintenance mechanic	17	0.81—0.08	0.17	0.12	0.18	44.38—0.19	3.15	0.34	3.39
Carpenter	4	0.11—0.10	0.11	0.11	0.11	30.60—0.20	7.80	0.20	7.73
Common laborer	17	12.33—0.10	3.00	0.61	3.12	8.22—0.17	1.52	0.44	1.63
Instrument man	3	1.44—0.09	0.65	0.41	0.64	174.14—0.17	58.62	1.56	58.58

EPIDEMIOLOGIC INVESTIGATION IN THE REINFORCED PLASTICS INDUSTRY

As stated earlier, it was decided by NIOSH that a second epidemiologic study focusing on workers with a high occupational exposure to styrene and few concomitant chemical exposures should be undertaken. Three distinct industrial settings, styrene and polystyrene manufacturing, polystyrene fabrication, and reinforced plastics production, were identified. It was determined during plant visits in these three settings that styrene and polystyrene manufacturing and polystyrene fabrication are not labor intensive and represent low potential for worker exposure. The reinforced plastics production industry, on the other hand, has a large number of workers potentially exposed to higher concentrations of styrene. Therefore, this environment probably represents the best opportunity to evaluate qualitatively any potential health risk.

The reinforced plastics industry in the United States developed during World War II with the demand for rigid materials of high strength and low weight. This industry has rapidly expanded from a production level of 3,402 t of reinforced plastics in 1945 to an estimated 795,614 t in 1977. It has been projected that this industry will continue to expand at an average annual growth rate of 15 % through 1981 (14). The Reinforced Plastics and Composite Institute of the Society of Plastics Industry has estimated that between 60,000 and 120,000 people work in the U.S. reinforced plastics industry.

After the various processes used to make reinforced plastic products within the United States were evaluated, the reinforced plastics boatbuilding process was selected for study. This process was selected because of its relatively long operational history compared to most reinforced plastic processes and because of the high potential for worker exposure to styrene.

Method of study and efforts to identify cohort

The epidemiologic method which will be used in this study is the same as that used

in the study of the styrene-butadiene rubber industry — a retrospective cohort mortality study. The reinforced plastic boatbuilding industry did not begin full operation until the mid to early 1950s and tends to be comprised of modest-sized operations (facilities with 200 to 300 employees or fewer). Before a statistically meaningful number of person-years at risk can be obtained, the working population from several facilities with a relatively long operational history will need to be included in the study. Additionally, these person-years at risk must have occurred long enough in the past to allow for clinical manifestation of any chronic health problems associated with occupational exposure.

The preliminary field visits were made to the larger boat manufacturing facilities in the state of Washington. Based on the information gathered at these plants, it has been determined, so far, that the workers from two facilities could be identified and included in the study population. The number of production workers currently employed in one of these plants is approximately 290 and has grown constantly since the start of the operations in 1952. The other facility began operation in the mid 1950s with a work force that has steadily expanded over the years to a current population of 485 individuals. To increase the size of the cohort, additional boatbuilding facilities are being identified for inclusion in the study.

Process and chemical hazards

Before the manufacturing process can be initiated, a prototype hull or deck which is made of wood, fiber glass, and resins is produced. The prototype is an exact duplicate of the reinforced fiber glass boat which is to be produced. This prototype is used to make a mold by building up layers of fiberglass cloth and polyester plastic on its surface.

The interior surface of the mold has the exact shape of the exterior of the boat being built. The mold is waxed on the inside before the manufacturing process starts. The manufacturing process begins with a worker spraying the inside of the

mold with a substance known as gelcoat, which makes up the smooth solid surface of the boat's exterior. Next, layers of fiber glass and polyester resins are applied by spray gun and by hand. The reinforced fiber glass is rolled, brushed, and squeegeed to work out airpockets and other imperfections. At this point the structure of the hull and deck has been formed. The resin and fiber glass are cured while on the mold for a prescribed amount of time, and then the deck or hull is taken off the mold and is ready for finishing (8).

The following description outlines the chemistry of the reinforced plastic process. The basic reaction is the polymerization of an organic acid and alcohol to form an ester. Styrene monomer is used in the reaction as a solvent and a reactant (8). It is a solvent because it dilutes the acid and alcohol and thereby keeps them in solution until mixed with a catalyst. Styrene is also a reactant because the soluble polymers formed by the acid and the alcohols are cross-linked (i.e., connected by styrene) to produce polymers which are insoluble in most common solvents. Prior to the formation of these insoluble polymers, the chemicals are mixed with glass fibers so that the desired end product is produced (15).

The major chemical hazard resulting from the handling and application of reinforced plastics is associated with styrene. Styrene comprises 40 % or more of the gelcoat and the resin, and is a volatile substance under normal conditions (9). Exposure to styrene can occur through several different routes: inhalation of atomized mist from the spray gun, dermal absorption during the hand work-up of the resin and fiber glass, and inhalation of styrene vapor evaporated during the curing process.

In my concluding remarks I would like to mention several additional ongoing epidemiologic investigations which may be pertinent:

1. In the United States the Society for the Plastics Industry (SPI) is conducting a cross-sectional medical study on approximately 300 active and a few retired employees at a reinforced plastic boat plant.

2. SPI is also considering the feasibility

of having a mortality study conducted in various segments of the reinforced plastics industry.

3. In addition Dr. Ahlmark from Sweden is currently conducting mortality and carcinogenic assessments of reinforced plastics workers from a number of plants. The assessments are based on national record systems and cancer registries in Sweden.

At this point, NIOSH would like to solicit any comments or suggestions on how these ongoing studies or new epidemiologic studies could better address the important questions raised so far at this conference. NIOSH is also interested in learning about any further epidemiologic research being conducted by governmental agencies, labor associations, or private industries in other countries.

REFERENCES

1. ALIMONA, S. T. Occupational hygiene and conditions of workers' health in preparation shops of fine factories. *Gig. tr. prof. zabol.* 15 (1971): 4, 24—28.
2. LEIBMAN, K. C. and ORTIZ, E. Epoxide intermediates in microsomal oxidation of olefins to glycols. *J. pharmacol. exp. ther.* 173 (1970) 242—246.
3. LIFELINES, OCAW HEALTH AND SAFETY NEWS. Update on leukemia investigation among SBR workers. *Lifelines, OCAW health and safety news* 24 (1977): 4.
4. LILIS, R. and NICHOLSON, W. J. Cancer experience among workers producing styrene monomer. In: *Proceedings of NIOSH styrene-butadiene briefing, April 30, 1976.*
5. LOPRIENO, N., ABBONDANDOLO, A., BARALE, R., BARONCELLI, S., BONNATI, S., BRONZETTI, G., CAMMELLINI, A., CORSI, C., CORTI, G., FREZZA, D., LEPORINI, C., MAZZACCARO, A., NIERI, R., ROSELLINI, D. and ROSSI, A. M. Mutagenicity of industrial compounds: Vinyl chloride, styrene and their possible metabolites. *Mutat. res.* 38 (1976) 114—115.
6. MC CANN, J. Detection of carcinogens as mutagens in Salmonella microsomal test. *Proc. nat. acad. sci. u.s.a.* 73 (1976) 950—954.
7. MC MICHAEL, A. J., SPIRTAS, R., GAMBLE, J. F. and TOUSEY, P. M. Mortality among rubber workers: Relationship to specific jobs. *J. occup. med.* 18 (1976): 3, 178—183.

8. MILLER, S. Manufacturing process descriptions (reinforced plastic boats). Glasstron Boat Company, Austin, Texas 1972, pp. 1—3.
9. MILLER, S. Manufacturing process descriptions (reinforced plastic boats). Glasstron Boat Company, Austin, Texas 1972, p. 4.
10. MILVY, P. and GARRO, A. J. Mutagenic activity of styrene oxide (1,2 epoxyethylbenzene), a presumed styrene metabolite. *Mutat. res.* 40 (1976) 15—18.
11. SALTMAN, W. M. Butadiene polymers. In: *Encyclopedia of polymer science and technology*, Interscience Publishers 1965.
12. SALTMAN, W. M. Styrene-butadiene rubbers. In: M. MERTON (ed.), *Rubber technology*. Van Nostrand Reinhold Company, New York, N. Y. 1973, pp. 178—198.
13. SHREVE, R. M. *Chemical process industries* (3rd ed.). McGraw-Hill Book Company, New York, N.Y. 1967.
14. SOCIETY OF THE PLASTICS INDUSTRY INC., REINFORCED PLASTICS/COMPOSITES INSTITUTE. *Guidelines for manufacture of reinforced plastics/composites*. New York, N.Y. 1977, pp. 1—3.
15. SOCIETY OF THE PLASTICS INDUSTRY, INC., REINFORCED PLASTICS/COMPOSITES INSTITUTE. *Guidelines for manufacture of reinforced plastics/composites*. New York, N.Y. 1977, pp. 6—7.
16. VAINIO, H., PÄÄKKÖNEN, R., RÖNNHOLM, K., RAUNIO V., and PELKÖNEN, O. A study of the mutagenic activity of styrene and styrene oxide. *Scand. j. work environ. & health* 2 (1976) 147—151.

QUESTIONS AND ANSWERS

Question to Mr. MEINHARDT and Dr. FISCHBEIN

Dr. A. LEHTNIEMI:

Upper respiratory tract infections are more common in employees exposed to various chemicals in the rubber and plastic industries, including styrene-butadiene-acrylonitrile; on the other hand, viral etiology has been proposed for human leukemia. Have you taken into account the frequency and type of respiratory infections among those workers who died to leukemia or lymphoma? In other words, the high incidence in leukemia could be an indirect effect related to irritative properties and not to mutagenic properties of styrene. (all "flu" will never be recorded!)

Mr. MEINHARDT:

In the ongoing NIOSH epidemiologic study of SBR workers, this hypothesis has not been considered to date, but it is very interesting. Respiratory health hazards in this industry are of interest, and the analysis of mortality patterns in this investigation will pay specific attention to respiratory problems.

Dr. FISCHBEIN:

The causal relationship between respiratory infections and leukemia is well known, since patients with leukemia have a decreased resistance to infectious diseases in general. This may be due to impaired function of leucocytes or impairment of immunological competence. This is a *post facto* phenomenon, however.

In our clinical, cross-sectional study there was a higher prevalence of respiratory symptoms among those with high exposure than among the workers with low exposure.

In addition there was a trend towards a higher prevalence of pulmonary function abnormalities ($FEV_1/FVC < 0.75$) among workers with higher urinary mandelic acid excretion.

With regard to the mortality study I have no information about the incidence of respiratory infections among the individuals who subsequently developed leukemia. It seems that it would be very difficult to obtain accurate data on this matter in a retrospective-prospective study. Generally, there was a very low mortality in respiratory disease in the mortality study presented (1 case observed against 7 expected).