Clinical Studies of Styrene Workers: Initial Findings

by William V. Lorimer,* Ruth Lilis,* William J. Nicholson,* Henry Anderson,* Alf Fischbein,* Susan Daum,* William Rom,* Carol Rice,* and Irving J. Selikoff*

Styrene monomer is a high volume chemical used chiefly in production of polystyrene. A clinical survey of 493 production workers was undertaken at the oldest and largest monomer production, polymerization, and extrusion facility in the U.S. Relative exposure durations and levels were obtained from occupational histories. Significant differences between the high and low exposure groups were found with regard to history of acute prenarcotic symptoms, acute lower respiratory symptoms, prevalence of FEV₁/FVC < 75%, and elevated GCTP. Other liver function tests, chest x-ray, FVC < 80%, and hematological parameters showed no distinct pattern. A concomitant mortality study has been mounted and is in progress.

About 2.8 million tons of styrene were produced in the United States in 1973, slightly less than toluene and slightly more than vinyl chloride (1). Polystyrene and styrene polymers (butadiene–styrene, acrylonitrile–butadiene–styrene for example) production totaled 2.2 million tons in 1974 and was expected to rise to 11 millions tons by the year 2000 (2). The other major use of styrene is as a crosslinking agent in polyester resin manufacture; 30–40% of the volume of fresh resin may be styrene (3).

Physically, styrene monomer is a volatile liquid (see Table 1); most human exposure is to this form. During the commonly used hand layup glass fiber–polyester resin process, evaporation rates of styrene are on the order of 50 g/m² in 30 min; exposures are of the order of 100–200 ppm (3–5) time-weighted average (TWA) over a several hour period. Levels in styrene production or polymerization are less readily obtained. Barcotti (6) gave a level of 192 ppm during polymerization, 25–50 ppm for other tasks. In addition, heating commercial polystyrene may give off styrene in amounts up to several hundred to a few thousand parts per million (7,8).

The partition coefficient of styrene favors steady-state concentrations which are highest in fat and decrease progressively from fat to blood to water to air (9,10) (Table 1). Styrene has been found in the fat of occupationally exposed workers (11).

Table 1. Properties of styrene monomer.

| Property                      | C₆H₅—CH=CH₂ |
|-------------------------------|-------------|
| Structure                     |             |
| Freezing point, °C            | 30.6        |
| Boiling point, °C             | 145.2       |
| Vapor pressure at 25°C, mm Hg| 6.1         |
| Air saturated with styrene at 25°C, ppm | 8026 |
| Vapor density                | 3.6         |
| Explosive limits, ppm        | 11,000–61,000 |
| Conversion factor            | 1 ppm = 4.2 mg/m³ |
| Water solubility, mg/l.      | 300         |
| Miscible in common organic solvents |            |

Partition coefficients:

|                     |             |
|---------------------|-------------|
| Water/air           | 4.38        |
| Blood/air           | 32          |
| Oil/blood           | 130         |
| Oil/air             | 4160        |

* Environmental Sciences Laboratory, Department of Community Medicine, Mount Sinai School of Medicine of the City University of New York, New York, N. Y. 10029.
Dynamically, styrene is well absorbed through the lungs (about 70–90% of that contained in the alveolar ventilation) \((12,13)\). Over a concentration range of 0–350 ppm and over a period of several hours, the same proportion of inspired styrene continues to be absorbed \((12)\). Styrene is also well absorbed through the skin \((14)\). Blood styrene continues to rise over time during this period \((13,15)\).

Styrene is metabolized in man (about 1% expired unchanged) to a mixture of hippuric, phenylglyoxylic, and mandelic acids \((16)\) which are excreted in the urine. The primary metabolic pathway is outlined in eq. (1). Liebman \((17)\) reviewed the pathway and summarized the evidence for styrene oxide being the first metabolic step.

\[
\begin{align*}
\text{Styrene} & \rightarrow \text{Styrene oxide} & \text{Styrene glycol} \\
R-\text{CH}-\text{CH}_2 & \rightarrow R-\text{CH}-\text{CH}_2 & R-\text{CH}-\text{CH}_2 \\
\text{OH} & \rightarrow \text{OH} & \rightarrow \rightarrow \rightarrow
\end{align*}
\]

\[
\begin{align*}
\text{Mandelic acid} & \rightarrow \text{Phenylglyoxylic acid} \\
\text{OH} & \rightarrow \text{O} \\
R-\text{COOH} & \rightarrow R-C-COOH \\
\text{Hippuric acid} & \rightarrow \text{Hippuric acid} \\
R-C-NH-CH & \rightarrow R-C-NH-COIH \\
\text{Benzoic acid} & \rightarrow \text{Benzoic acid} \\
\text{glycine} & \rightarrow \text{CO}_2
\end{align*}
\]

(1)

Styrene oxide has been shown to be a base-substitution mutagen; other metabolites were not found to be mutagenic \((18)\). The evidence for the mutagenicity of styrene itself is mostly negative \((18)\); however, Vainio \((19)\) has stated that styrene may be mutagenic in the presence of a microsomal system. It may be that styrene oxide is produced by microsomes.

The metabolism of styrene takes place in the liver; it is stimulated by phenobarbital and suppressed by coadministered toluene \((20)\). At low level styrene exposure \((1–50 \text{ ppm over few hours})\) an increase in mandelic acid excretion in the urine is detectable \((4,16,21–23)\), peaking about 4–5 hr after a 1–2 hr exposure. At high level exposure of about 100 ppm TWA \((4,16)\), the excretion rate of the metabolites reaches a plateau. A significant increase in hippuric acid excretion occurs \((16,24)\), an observation first noted for high exposure in 1944 \((24)\). This peak of hippuric acid excretion rate is delayed for about 20 hr \((16)\).

Toxicology

The toxic effects of styrene were first reported for acute and chronic exposures in 1942 \((25)\). At exposures of 5000 ppm, most animals were unconscious within 1 hr and all died within 8 hr of apparent CNS depression. At exposures of 1300 ppm, a small proportion of rats and all guinea pigs died after 40 hr of continuous exposure of pulmonary edema. Acute liver and kidney damage were also noted. At 1300 ppm for 8 hr daily, 5 days per week for 6 months, 10% of guinea pigs died of pulmonary irritation within a few days. Slight increase in weight of liver and kidney was noted for rats. Eye and nose irritation was common at 1300 ppm and present at 650 ppm. Hematological values were not altered. Lifetime studies were not done. Gut \((26)\) found that the spontaneous motor activity in the rat decreased at levels of several hundred ppm for 8 hr.

Studies in humans (see Table 2) have found related effects in acute experiments lasting a few hours at 800 ppm \((24)\). The subjects were grossly unsteady and drowsy, with nasal and eye irritation and a metallic taste in the mouth. They felt tense and depressed. In the range of 350 ppm irritation was still strong, and objective tests of coordination and dexterity \((15)\) and reaction time were abnormal. Gamberale \((27)\) also found that subjects felt affected and tense after exposure. At a level of 200 ppm, Oltramare \((18)\) found increased reaction times in 30%; Gamberale \((27)\) found no change. Irritative symptoms were present to 50–100 ppm \((13,15)\), reaction time increases and subjective symptoms were inconsistently present \((13,15,27)\). Odor was noted to levels of 3–5 ppm, but irritation, increased reaction time, and subjective symptoms \((13)\) were absent. Acute pulmonary function changes, or acute liver function changes have not been systematically examined in human subjects.
Table 2. Toxic effects of styrene in humans.

| Reference                  | Number examined | Process resin/rubber | Dose, ppm × yr | Effects                                                                 |
|----------------------------|-----------------|----------------------|----------------|--------------------------------------------------------------------------|
| Barsotti, 1952             | 41              | Monomer manufacture, polymerization | 24–196 × years | Slight leucopenia, relative lymphocytosis, irritation, decreased night vision, urinary hippuric acid normal |
| Katz, 1962                 | 526             | Rubber               | ca. 20 × years | Hepatomegaly (30%), splenomegaly (6%), increased bilirubin (80%), leucopenia (30%), reticulocytosis (59%) |
| Zielhuis, 1962             | 55              | Resin                | 10–200, up to 5 yr | Hematological normal, differential normal, irritation, drowsiness |
| Pratt-Johnson, 1964        | 1               | Resin                | Unknown × 5 yr | Retrolublar neuritis, reverting after one year, headache, sleepiness, dyspepsia |
| Huzel, 1967                | 55              | Resin                | 50–100 × yr | Weltman reaction 48% Hematology normal |
| Benini, 1970               | 99              | Rubber               | Unknown        | High red blood count, high siderocytes |
| Araki, 1971                | 1               | Resin                | Unknown × 14 yr | Peripheral neuropathy, EMG abnormal, EEG normal, hematology normal, liver normal, skin atrophy |
| Gotell, 1972               | 12              | Resin                | 100–200 × years | Increased reaction time, urine mandelic acid elevated |
| Klimokova-Deutskhova, 1973 | 105             | Resin                | Unknown × years | Headache, sleepiness, peripheral neuropathy, EMG, deteriorating EEG, nystagmus, facial palsy |
| Chemielewski, 1973         | 101             | Resin                | Unknown × years | Blood protein, lipid normal above average, glucose tolerance |
| Oltramare, 1974            | 5               | Resin                | 20–560 × years | 3/5 increased bilirubin, 2/5 wbc below 5000 |

Styrene effects have been most widely studied in the use of polyester resin to make laminates (glass fiber) or related processes (3,5,13,28–31). Some have studied copolymer production in synthetic rubber manufacture (32–33). A summary of a number of studies is given in Table 2. Studies of styrene manufacturing and polymerization factory were reported only by Barsotti (6) in 1952. He found irritation, especially of skin and eyes, and complaints of decreased night vision. A slight leucopenia was present in some workers, possibly related to the presence of benzene in the plant. Katz (33) showed a high prevalence of liver and hematological changes in a synthetic rubber manufacturing plant.

Zielhuis (3) in reviewing the literature in 1962, stated that irritation of mucosa and non-specific asthenia and lassitude were commonly found associated with industrial exposures to styrene. Hematological abnormalities were in

Table 3. Sex and age distribution of styrene workers.

| Age     | Number | %  |
|---------|--------|----|
| <21     | 3      | 0.6|
| 21–30   | 104    | 21.1|
| 31–40   | 118    | 23.9|
| 41–50   | 82     | 16.6|
| 51–60   | 107    | 21.7|
| 61–70   | 61     | 12.3|
| 71+     | 15     | 3.0 |
| Unknown | 4      | 0.8|
| Total   | 494    | 100.0|

| Sex     | Number | %  |
|---------|--------|----|
| Male    | 485    | 98.2|
| Female  | 9      | 1.8 |
| Total   | 494    | 100.0|
that Eastern European authors regard the toxicity of styrene as serious, finding abnormalities in the central nervous system, hematological system, and liver. Zlobina in 1971 (34) reflected this continuing concern over low styrene concentrations.

Current Investigation

A styrene monomer and polymerization plant was studied, in which a large number of workers had had relatively pure styrene exposure for many years. This paper reports initial clinical findings in 494 workers. An investigation of the mortality experience of 563 long-term styrene workers is also currently underway.

The plant began in 1943 as a production facility for butadiene and styrene (see Fig. 1), manufacturing the monomers but not copolymerizing them. Butadiene was produced until about 1950. Styrene and butadiene were polymerized elsewhere into butadiene rubber. Since the 1950's the principal product has been polystyrene. Limited extrusion of polystyrene also is undertaken; the remainder of the polystyrene is extruded elsewhere. Over 90% of the polystyrene coffee cups in the United States comes from polystyrene manufactured in this plant. Since 1969 ethylbenzene has been the starting product. Little benzene has been present and that in specific areas, notably the benzene building and styrene monomer purification areas (see Fig. 2). Significantly less benzene exposure occurred during the 1963–1975 period. Some toluene is recovered, primarily as a side product of the ethylbenzene-styrene conversion process. About 650 workers are employed in production. Approximate numbers employed in each area are noted in Figure 2, e.g., about 20 workers are involved in storage of ethylbenzene, 200 in conversion of 99% + pure styrene to polystyrene. Most of the end product is polystyrene beads (polystyrene impregnated with various pentanes). When the "beads" are heated and extruded, they expand to polystyrene foam used for coffee cups and other articles. Off-quality beads are processed at the plant to foam trays, used primarily in the retail packaging of meat.

Characteristics of Group

The group examined numbered 494. The median age was in the 40's, but because of hiring practices in the past, the distribution is bimodal (see Table 3). Males constituted 98% of the group. Table 4 shows in which year each of the workers was first employed. Relatively few workers were first employed in the late 1950's and early 1960's.

![Figure 2. Current styrene production.](image)

![Figure 1. Plant history.](image)

### Table 4. Year of first exposure of styrene workers.

| Year    | Number | Distribution |
|---------|--------|--------------|
| <1950   | 112    | 22.7         |
| 1950–54 | 94     | 19.0         |
| 1955–59 | 25     | 5.1          |
| 1960–64 | 7      | 1.4          |
| 1965–69 | 109    | 22.1         |
| 1970+   | 147    | 29.8         |
| Total   | 494    | 100.0        |
Table 5. Information gathered.

| Test information                                                                 | Proportion done; selection | Purpose                                                                 | Organ system                  |
|----------------------------------------------------------------------------------|-----------------------------|-------------------------------------------------------------------------|-------------------------------|
| Basic demographic data (age, sex, height, weight)                                | All                         | Standardization of tests, particularly pulmonary function               | Liver                         |
| Blood chemistries (25)                                                           | All                         | Routine screen; special emphasis on liver                                | Lung, liver, other malignancy |
| CEA                                                                              | All                         | To select those with higher possibility for developing carcinoma         |                               |
| Styrene                                                                          | All                         | Test system for detection of styrene in low blood concentration; possible validation of occupational history categories |                               |
| Urine, protein, glucose                                                          | All                         | Routine screen                                                           | Kidney, endocrine             |
| Urine, mandelic, phenylglyoxidic, and hippuric acid                               | All                         | Styrene metabolites, test of methodology; possible validation of occupational history categories |                               |
| Sputum, cytology                                                                 | All smokers plus nonsmokers over 40 | Screen for increased atypia and malignancy                             | Lung                          |
| Occupational history (complete lifetime history up to last shift worked)          | All                         | Determine specific exposure; last shift history to be related to urine metabolite levels |                               |
| Medical history                                                                  | All                         | Elimination of effects caused by known medical conditions               | Cardiopulmonary               |
| Respiratory history, standard questionnaire                                      | All                         | Enables other variables to be controlled for cigarette smoking          | Eye, ENT, respiratory CNS     |
| Special questionnaire, acute symptoms                                            | All                         | Possible acute symptoms related to styrene-irritative, prenarcotic      | Nervous system, liver, spleen, pulmonary, ENT |
| Physical examination                                                             | All                         | Chest, abdomen, peripheral nervous system especially                     |                               |
| Ophthalmological examination                                                      | All                         | Screening exam; external examination                                     | Eye                           |
| Chest x-ray                                                                      | All                         | General screen; ILO U/C pneumonocnosis reading                           | Lung, heart                   |
| Spirometry                                                                       | All                         | FEV, FVC, flow at 25% of volume, FEF (25-75%)                            | Lung                          |
| Codiffusion                                                                      | 60 unselected               | CO diffusing capacity, single breath                                     | Lung                          |
| Reaction time                                                                    | Unselected                  | Simple reaction time                                                     | Nervous system                |
| Nerve conduction velocity                                                         | 100 selected                | Multiple conductions, lower and upper extremities                        | Peripheral nervous system     |
| Fat aspiration                                                                   | 25 selected                 | Fat level of styrene, ethylbenzene, toluene                             |                               |
| Hemogram, platelets                                                              | All                         | See if abnormality relates to benzene or styrene areas                   | Hematological                 |
| Urine, mutagenic                                                                 | 30 selected                 | Possible effect on genetic material                                     | DNA                           |
| Chromosome morphology                                                            | 10 selected                 | Possible effect on genetic material                                     | DNA                           |

**Studies Undertaken**

Table 5 summarizes the information gathered during this examination. Selection was governed by trying to achieve clinical breadth while also trying to test hypotheses gleaned from literature review and from interviewing workers and management personnel prior to the examination. It is evident that the scientific emphasis of this survey was upon hypothesis development rather than hypothesis testing.
This report will deal with prevalence of certain symptoms (prenarcosis, acute irritation, those of chronic bronchitis) and test results (simple spirometry, chest x-ray, serum liver enzymes, hemogram, and platelet count). The above parameters will be related to estimated styrene exposure.

From review of job descriptions and actual tasks performed by those in each job, an estimate of relative exposure was obtained (see Table 6). In developing this estimate, we utilized the experience of management and of workers and had available a NIOSH Health Hazard Evaluation (35) of the facility. Of the 488 production and maintenance members for which adequate occupational histories are available, 200 were judged currently to be in low exposure, and 288 in relatively high styrene exposure. Significant benzene exposure was thought to be a possibility in certain job categories, as marked. Analysis is by relative exposure and time. High exposure is defined as 80% or more of years having been spent in a high exposure job. The level of 90% has been used as the dividing line for history of acute symptoms.

Results

Styrene at high concentrations (hundreds of ppm) produces a prenarcotic syndrome, described by the individual affected as being "lightheaded" or "drunk." An attempt was made to exclude prenarcosis due to other substances (such as pentane) which also cause the syndrome. Of the workers 13% overall had had at least one episode of prenarcosis (see Table 7). Those with high styrene exposure had significantly more prenarcosis than those with low exposure.

Table 6. Occupational distribution of high and low styrene exposure.

| Distribution, no. | Low exposure (total 200) | High exposure (total 288) |
|-------------------|--------------------------|--------------------------|
|                   | Retired or working elsewhere | Handling of extruded polystyrene or finished beads |
|                   | Power house | Sheet plant | Polystyrene handler |
|                   | Handling and transportation, miscellaneous packaged materials | Maintenance, low exposure | Other |
|                   | Production: | Styrene manufacture | Styrene purification |
|                   | | Styrene polymerization | To polystyrene |
|                   | | To copolymers, special processes | Miscellaneous production workers |
|                   | Maintenance: | Pipe fitters | Millwrights |
|                   | | Electrician | Laborer |
|                   | | Welder | Other |
|                   | Other high exposure | 41 | 22 |
|                   | 22 | 41 | 16 |
|                   | 25 | 22 | 22 |
|                   | 11 | 16 |

Table 7. Acute prenarcotic symptoms in styrene-exposed workers.

| History of prenarcotic symptoms | 0.1-7.0 yr | 7.1-20 | >20.0 yr | Total |
|-----------------------------|------------|--------|----------|------|
| Low                         | 15/143 (10%) | 2/61 (3.3%) | 13/102 (13%) | 30/306 (10%) |
| High                        | 3/34 (9%) | 11/53 (21%) | 20/95 (21%) | 34/182 (19%) |
| Total                       | 18/177 (10%) | 13/144 (11%) | 33/197 (17%) | 64/488 (13%) |

*Significance for high as compared with low: $\chi^2 = 7.81, 0.001 < p < 0.01; \chi^2 = 0.08, NS (0.1-7.0 yr); \chi^2 = 8.57, 0.001 < p < 0.01 (7.0-20.0 yr); \chi^2 = 2.43, NS (>20.0 yr).

Acute mucous membrane irritation is a common occurrence above levels of 50–100 ppm in experimental work with subjects never before exposed to styrene. Significant tolerance may develop in industrial populations. This fact may explain our failure to find differences in prevalence between relatively high and low styrene (see Table 8).

The workers were also asked if they ever had wheezing or tightness in the chest from styrene vapors. In this case 11% of workers had such an episode. Significantly more high than low exposed workers had had this symptom (see Table 9).
Table 8. Mucous membrane irritation in styrene-exposed workers.

| Styrene exposure | 0.1–7.0 yr | 7.1–20 yr | >20.0 yr | Total  |
|------------------|------------|-----------|----------|--------|
| Low              | 28/143     | 6/61      | 17/102   | 51/306 |
|                  | (20%)      | (10%)     | (17%)    | (17%)  |
| High             | 4/34       | 11/53     | 22/95    | 37/182 |
|                  | (12%)      | (21%)     | (23%)    | (20%)  |
| Total            | 32/177     | 17/114    | 39/197   | 88/488 |
|                  | (18%)      | (15%)     | (20%)    | (18%)  |

The prevalence of chronic bronchitis was investigated (see Table 11); 19% of the workers reported such symptoms.

Table 11. Chronic bronchitis in styrene-exposed workers.

| Styrene exposure | 0.1–7.0 yr | 7.1–20 yr | >20.0 yr | Total  |
|------------------|------------|-----------|----------|--------|
| Low              | 6/83       | 7/61      | 22/78    | 35/222 |
|                  | (7.2%)     | (11%)     | (28%)    | (16%)  |
| High             | 9/61       | 17/70     | 28/119   | 54/250 |
|                  | (15%)      | (24%)     | (24%)    | (22%)  |
| Total            | 15/144     | 24/131    | 50/197   | 89/472 |
|                  | (10%)      | (18%)     | (25%)    | (19%)  |

* Definition: cough and sputum production on most days for at least 3 months for at least 2 yr.

To eliminate the effect of smoking, nonsmokers were analyzed separately (see Table 12). Of the nonsmokers, 6% had symptoms consistent with chronic bronchitis. No trends were noted. We have seen such findings in other industrial populations. It is questionable whether styrene exposure had etiological importance in this population.

Table 12. Chronic bronchitis in nonsmoking styrene-exposed workers.

| Styrene exposure | 0.1–7.0 yr | 7.1–20 yr | >20.0 yr | Total  |
|------------------|------------|-----------|----------|--------|
| Low              | 2/19       | 2/18      | 0/13     | 4/50   |
|                  | (11%)      | (11%)     | (0%)     | (8%)   |
| High             | 1/15       | 0/15      | 0/23     | 1/53   |
|                  | (7%)       | (0%)      | (0%)     | (2%)   |
| Total            | 3/34       | 2/33      | 0/36     | 5/103  |
|                  | (9%)       | (6%)      | (0%)     | (5%)   |

* Definition: cough and sputum production on most days for at least 3 months for at least 2 years.

The prevalence of airway obstruction defined as FEV1/FVC < 75% was also investigated (see Table 13). Overall, 35.3% satisfied this criteria for obstruction; here, the high and low styrene groups were statistically different. Of the nonsmokers, 31.6% had evidence of airways obstruction (see Table 14), although no
pattern consistent with a simple dose-response relationship was present. As expected, obstruction increased with years on the job among smokers (see Table 15). Overall, 5.9% of the men had FVC < 80% predicted (see Table 16); restriction was not of significance in this group of workers.

Table 13. Airway obstruction (FEV₁/FVC < 75%) in styrene-exposed workers.¹

| Styrene exposure | Prevalence of airway obstruction ¹ |  |
|------------------|----------------------------------|---|
|                  | 0.1-7.0  | 7.1-20  | >20.0  | Total  |
| Low              | 17/82    | 18/60   | 36/72  | 71/214 |
|                  | (21%)    | (30%)   | (50%)  | (33%)  |
| High             | 15/60    | 27/69   | 50/108 | 82/287 |
|                  | (25%)    | (39%)   | (46%)  | (39%)  |
| Total            | 32/142   | 45/129  | 86/180 | 163/451|
|                  | (23%)    | (35%)   | (46%)  | (35.2%)|

¹ FEV₁-forced expiratory volume at 1 sec; FVC-forced vital capacity.

² Significance for low styrene exposure as compared with high styrene exposure: χ² = 2.17, not significant (NS).

Table 14. Airway obstruction (FEV₁/FVC < 75%) in nonsmoking styrene-exposed workers.

| Styrene exposure | Prevalence of airway obstruction ¹ |
|------------------|----------------------------------|
|                  | 0.1-7.0  | 7.1-20  | >20.0  | Total  |
| Low              | 5/19     | 6/18    | 7/13   | 18/50  |
|                  | (26%)    | (33%)   | (54%)  | (36%)  |
| High             | 5/15     | 3/15    | 5/23   | 13/53  |
|                  | (33%)    | (20%)   | (22%)  | (25%)  |
| Total            | 10/34    | 9/33    | 12/36  | 31/103 |
|                  | (29%)    | (27%)   | (33%)  | (30%)  |

² Significance for low styrene exposure as compared with high styrene exposure: χ² = 1.46 (NS).

Table 15. Airway obstruction (FEV₁/FVC < 75%) in smoking styrene-exposed workers.

| Styrene exposure | Prevalence of airway obstruction ¹ |
|------------------|----------------------------------|
|                  | 0.1-7.0  | 7.1-20  | >20.0  | Total  |
| Low              | 8/49     | 10/29   | 21/34  | 39/112 |
|                  | (16%)    | (34%)   | (62%)  | (35%)  |
| High             | 8/40     | 17/43   | 21/41  | 46/124 |
|                  | (20%)    | (40%)   | (51%)  | (37%)  |
| Total            | 16/89    | 27/72   | 42/75  | 85/236 |
|                  | (18%)    | (38%)   | (56%)  | (36%)  |

² Significance for low styrene exposure as compared with high styrene exposure: χ² = 0.13 (NS).

The x-rays were categorized by the ILO-U/C International Classification of Radiographs of Pneumoconiosis (see Table 17). Apart from those with history of previous coal or asbestos exposure there was no finding of significant radiological change; surely not at the level we have seen in vinyl chloride workers (31).

Table 17. Abnormal x-ray findings among styrene-exposed workers.²

| ILO U/C classification |
|------------------------|
| Styrene exposure       | 1/0-1/2 | 2/1-2/3 | 3/2-3/4 | Total |
| Low                    | 17/250  | 5/250   | 1/250   | 23/250 |
|                       | (6.8%)  | (2.0%)  | (0.4%)  | (9.2%) |
| High                   | 14/167  | 4/167   | 0/167   | 18/167 |
|                       | (8.4%)  | (2.4%)  | (0.0%)  | (11%)  |
| Total                  | 31/417  | 9/417   | 1/417   | 41/417 |
|                       | (7.4%)  | (2.2%)  | (0.21%) | (9.8%) |

² Excluding those with known prior exposure to asbestos or coal dust.

Hepatic function was investigated by using bilirubin, alkaline phosphatase, SGPT, GGTP, and SGOT as parameters (see Table 18). The distribution of the abnormal results was investigated. For this initial analysis, "abnormal" was defined as at or above the 96th percentile as compared with a group of 993 nonhospitalized men aged 40-44 tested at the same laboratory; 471 sets of results were available for analysis.

When tested for styrene (high and low) and duration, only GGTP showed a nonrandom pattern (see Table 19). Overall, 4.9% were elevated: 6.7% in the high styrene and 2.8% in the low styrene groups. This difference was statistically significant. The difference shown
in the > 20 and < 20 yr groups is significant but needs to be adjusted for age-dependent increase in GGTP. When those with alcohol consumptions of more than 400 proof ounces (2 oz pure ethanol) per week are excluded (see Table 20), the differences increase between the low and high styrene groups. For those currently working, those with low styrene and high styrene with concurrent relatively low and high benzene are compared (see Table 21). No comparisons reach statistical significance, although both chemicals may have an effect on the prevalence of GGTP. No other patterns were observed when we analyzed other liver function tests in a similar manner.

Table 19. Elevated GGTP in styrene-exposed workers.

| Styrene exposure | Incidence of elevated GGTP<sup>a</sup> |
|------------------|--------------------------------------|
|                  | 0.1–7.0  | 7.1–20  | >20.0  | Total |
| Low              | 1/83     | 1/60    | 4/75   | 6/218  |
|                  | (1.2%)   | (1.7%)  | (5.3%) | (2.8%) |
| High             | 1/62     | 2/72    | 14/119 | 17/253 |
|                  | (1.6%)   | (2.8%)  | (12%)  | (6.7%) |
| Total            | 2/145    | 3/132   | 18/194 | 23/471 |
|                  | (1.4%)   | (2.3%)  | (9.3%) | (4.9%) |

<sup>a</sup> Significance for high styrene compared with low styrene: \( \chi^2 = 3.98, 0.02 < p < 0.05 \); for over 20 yr compared with under 20 yr: \( \chi^2 = 13.72, p < 0.001 \).

Hematological parameters investigated included hemoglobin, white blood count, and platelet count (see Table 22): 13.6% of the workers had hemoglobin levels below 14.0 g-%; 2.7% had white blood counts below 4800; and 7.4% had platelet counts below 180,000. An-
Discussion

The results of this clinical survey confirm styrene to be an irritant of the mucous membranes of the upper respiratory tract. The possibility that styrene may also be a significant lower respiratory irritant in occupational groups must also be considered. That 30% of the nonsmokers had FEV₁/FVC < 75%, and that 12% of the high exposed workers (compared to 4% of the lower exposed) had repeated episodes of wheezing and/or tightness in the chest suggests an etiological relationship.

Serum γ-glutanyl transpeptidase was higher among those with higher exposure, consistent with hepatic changes. Hematological findings did not yield evidence of significant marrow depression in this preliminary analysis.

In comparison with findings of studies (36, 37) done in a similar manner of workers exposed to another monomer, vinyl chloride, there was no evidence of characteristic vinyl chloride monomer changes such as Reynaud’s syndrome,acroosteolysis, clinical hepatic disfunction, or skin changes No overt neoplasms were found in this survey.

Summary

Initial analysis of findings in a clinical survey of 494 workers at a styrene manufacturing, polymerization, and polystyrene extrusion facility has been undertaken. No unusual clinical patterns emerged, although styrene monomer is confirmed as an irritant and CNS depressant, and some changes in pulmonary function and in serum GGTP were found. An investigation of the mortality experience of workers at this facility is underway and will be reported later, as will findings of other studies performed during this survey of styrene-exposed workers.

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