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Mortality Among Rubber Chemical Manufacturing Workers

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Background *A retrospective cohort mortality study evaluated ischemic heart disease (IHD) among workers in the "rubber chemicals" manufacturing department of a Western New York plant. A previous study at the plant found elevated chest pain and angina among workers in this department.*

Methods *Mortality experience of workers employed from 1946–1988 was followed through December 31, 1994. Mortality was compared to U.S. population rates and to local Niagara county rates by using the NIOSH life table analysis system. Poisson regression was used to examine patterns of IHD within the cohort.*

Results *The standardized mortality ratio (SMR) for IHD among workers in the rubber chemicals department was 1.51 (U.S. rates) and 1.19 (Niagara county rates). Increased mortality from IHD in the rubber chemicals department was most pronounced at younger ages (< 50, SMR = 2.4); workers in a second chemical production department also had an elevated (but not statistically significant) SMR of 1.5 for IHD.*

Conclusions *IHD mortality among workers in the rubber chemicals department was elevated, particularly among those under 50 years of age. Potential occupational risk factors for IHD include the rotating shift pattern for employees assigned to two chemical production departments and chemical exposures present in the rubber chemicals department.* Am. J. Ind. Med. 37:590–598, 2000. *Published 2000 Wiley-Liss, Inc.*†

KEY WORDS: epidemiology; occupational cohort mortality; rubber manufacturing; ischemic heart disease

INTRODUCTION

In 1988, union representatives at an upstate New York chemical plant requested that the National Institute for Occupational Safety and Health (NIOSH) conduct a health hazard evaluation of bladder cancer incidence and cardiovascular disease among workers in a plant department that manufactured rubber chemicals [NIOSH, 1989]. The request mentioned that the union had observed an increased number of heart attacks, coronary by-pass operations, and elevated cholesterol levels among its members, and noted that members had exposure to carbon disulfide, aniline and a proprietary chemical, among other exposures. A previously reported study of bladder cancer incidence found 13 bladder cancers diagnosed between January 1, 1973 and January 1, 1989 among all 1749 workers who had been employed at the plant from 1946–1988, with only 3.61 expected (standardized incidence ratio (SIR) = 3.60; CI = 2.13–5.73) [Ward et al., 1991]. Seven of the cases occurred among workers assigned to the rubber chemicals department (SIR = 6.48; CI = 3.04–12.2).

A cross-sectional study [Oliver and Weber, 1984] had been conducted in 1980 at this plant to evaluate whether the prevalence of chest pain or coronary heart disease among workers from the rubber chemicals department exceeded

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that of a nonexposed group from the same plant. Oliver and Weber [1984] showed a relationship between chest pain and possible/definite coronary heart disease (CHD) and exposure to rubber chemicals. There was no relationship between CHD risk and duration of exposure. Other cardiovascular risk factors (i.e., smoking, blood pressure, and family history of heart disease) examined in the study were not found to account for the excess of incidence of chest pain and possible/definite CHD in workers exposed to rubber chemicals relative to an internal comparison group. Based on the results of this study, NIOSH investigators decided to evaluate heart disease via a cohort mortality study.

The chemical plant under study opened in 1946 for the production of polyvinyl chloride. Beginning in 1957, the plant made an antioxidant for use in tire manufacturing from *ortho*-toluidine (*o*-toluidine), aniline, hydroquinone, and toluene. A rubber accelerator was produced since 1970 from carbon disulfide, sulfur, aniline, benzothiazole, and a proprietary chemical. Workers in another department of the plant, which manufactured polyvinyl chloride, have been previously studied and found to have an excess risk of angiosarcoma of the liver [Nicholson et al., 1975, 1984].

The primary purpose of the retrospective cohort mortality study was to determine whether IHD mortality was elevated among workers in the rubber chemicals department; secondary purposes were to examine cancer mortality among workers both in the rubber chemicals department and in the polyvinyl chloride department.

STUDY POPULATION AND METHODS

Descriptions of the plant, processes and study design have been previously published [Ward et al., 1991]. The study population of 1749 workers was divided into three groups for analysis: (1) 708 workers ever employed in the rubber chemicals department (herein referred to as ''definitely exposed''; (2) 291 workers in maintenance, janitorial or yard work and shipping who had possible exposure to the rubber chemicals department (''possibly exposed''); and (3) all other workers (N = 750) who were not likely to have been exposed to the rubber chemicals department (herein referred to as ''probably not exposed''). Groups (1) and (3) were on 24 h a day, 7 days a week rotating shifts, rotating backward (i.e., evening to day) every week. To be consistent with previously published reports, analyses are presented by the three groups to examine differential exposure by department.

Standard life table analyses for the three groups were conducted by using the National Institute for Occupational Safety and Health (NIOSH) life table system (LTAS) [Steenland et al., 1990]. In these analyses, person-years at risk were distributed into categories by duration of employment in the specified departments, age, time since first exposure, and calendar time. Duration was defined as the total time a worker was employed in a given department. Time since first exposure was defined as the time since first hire into one of the selected departments that define the subcohorts. Cutpoints for duration of employment and time since first exposure, chosen a priori, were less than 5 years, 5–10 years, 10–15 years, 15–20 years, 20–25 years, 25–30 years, and 30+ years. Age and calendar year were categorized into 5-year intervals. Due to small numbers by race and gender, analyses are reported for combined race and gender categories. We report all-cause mortality, mortality from cancers (ICD 140–208, 9th revisions), and ischemic heart disease (IHD) mortality (ICD 410–414, 9th revision). Person-years began on January 1, 1957 (the year in which the rubber chemicals department was opened) or date first employed in the specified department and continued until either the date last observed or the study end date (December 31, 1994). All standardized mortality ratio (SMR) analyses reported in this paper are based on reference rates in the United States population. Comparisons to local mortality rates in Niagara County, New York were also conducted. Ninety-five percent confidence intervals (CIs) for reported SMRs were computed by using exact Poisson probabilities [Breslow and Day, 1987].

The potential contribution of a higher prevalence of cigarette smoking among plant workers compared to the U.S. reference population to elevated IHD mortality was evaluated by using a method described by Axelson and Steenland [1988]. As part of the prior study of bladder cancer incidence, a 5% sample of smoking histories of current and former workers was collected from plant medical records. Comparable smoking prevalence rates in the U.S. as of 1983 [DHHS, 1989] were directly standardized to the age distribution of the cohort. The use of rate ratios of 1.0 for those who had never smoked and 1.9 for current smokers were taken from Thun et al. [1995]; since this reference did not provide rate ratios for former smokers, it was assumed to be midway between the rate ratios of never and current smokers (1.45).

To further examine patterns of IHD mortality, internal comparisons were conducted by Poisson regression [Frome and Checkoway, 1985] by using the SAS PROC GENMOD procedure [SAS Institute, Inc., 1997]. Two-sided Wald confidence intervals for standardized risk ratios (SRR) were computed from Poisson regression model parameters. [SAS Institute, Inc., 1997]. In these analyses, the effects of age (<50 and 50+ years; <45 and 45+ years; <50, 50–59, and >60 years), time since first exposure (20+ years relative to <20 years), duration employed in specified departments (20+ years relative to <20 years), and calendar year (before or after 1985) on risk of mortality from IHD were evaluated by using Poisson regression models with a log-linear link function. Further evaluation of the effects of age and exposure group was done by fitting models with more than two age categories. Similarly, effects

of exposure duration and time since first exposure were examined by fitting models with more than two categories (< 5, 5–15, and > 15 years). Internal comparisons were made for the ''definitely exposed'' group versus the two other groups individually and combined. To evaluate whether a variable was an important predictor of ischemic heart disease risk, a series of nested models was fit and likelihood ratio tests were used to identify which parameters significantly improved the fit of the model to the data. Results for the life table SMR analyses are presented first, followed by the results of the internal comparison by using Poisson regression.

RESULTS

Overall Mortality

Table I describes general characteristics of the study population. Demographic and work history characteristics of the ''definitely exposed'' and ''probably not exposed'' groups were similar, while the ''possibly exposed'' group tended to have earlier dates of hire and therefore a larger proportion of workers (33%) with more than 10 years of employment. As of December 31, 1994, 83% of the ''possibly exposed'' and about 90% of the ''definitely exposed'' and ''probably not exposed'' cohort members were known to be alive (Table I). Table II presents overall mortality for selected causes among workers in each of the three groups compared to the U.S. population. The SMR for IHD among workers in the rubber chemicals department was 1.51 (95% CI = 0.94–2.3). An examination of SMRs for IHD by five year age categories showed statistically elevated risks for workers between the ages of 35–39 years (SMR = 6.54, 4 observed vs. 0.61 expected; 95% CI = 1.8–16.7). In life table analyses by using Niagara County referent rates, the SMR for all deaths among workers assigned to the rubber chemicals department (0.97; CI = 0.75–1.24) was similar to the SMR calculated by using U.S. referent rates (0.95; CI = 0.7–1.2), but the SMR for IHD was lower (SMR = 1.19; 95% CI = 0.75–1.8). The IHD SMR in the 35–39 year old age group remained significantly elevated (SMR = 4.78; CI = 1.3–12.2).

Among workers in the ''possibly exposed'' and ''probably not exposed'' groups, the SMRs for IHD based on U.S. referent rates were slightly greater than 1.0. However, when Niagara County rates were used, the SMRs for IHD among the ''possibly exposed'' and ''probably not exposed'' groups were below 1.0—0.82 (95% CI: 0.47–1.3) and 0.88 (95% CI: 0.55–1.3), respectively.

Other causes of death of a priori interest were malignant neoplasms of the bladder in the rubber chemicals department and malignant neoplasms of the liver in the polyvinyl chloride department. Among workers ''definitely exposed'' to the rubber chemicals department, there was one death from bladder cancer. There was also a significant increase in mortality from malignant neoplasms of ''other or unspecified sites'' (SMR = 3.9, 95% CI = 1.05–9.9) which appeared on the death certificates to be metastatic cancer

TABLE I. Characteristics of New York Rubber Manufacturing Cohort by Exposure Group

	Exposure group		
Characteristic	**Definitely exposed**	**Possibly exposed**	**Probably not exposed**
Number of workers	708	291	750
Deceased[a] (%)	65 (9.2)	48 (16.5)	78 (10.4)
Alive (%)	643 (90.8)	243 (83.5)	672 (89.6)
Average age (at death or last observed) [range]	47.5 [18–89]	54.5 [19–90]	48.4 [18–86]
% white	96.0	98.6	96.0
% male	96.5	94.8	91.2
Average year of first employment	1970	1962	1970
Average year of last employment[b]	1977	1975	1974
Average age at first employment	27.6	25.7	26.1
Cumulative employment[c] (%) [mean ± SD]	[2.8 ± 5.5]	[7.8 ± 10.1]	[4.8 ± 8.6]
< 5 years	82.2	58.1	76.3
5–10 years	7.3	9.3	5.5
10+years	10.5	32.6	18.2

[a]As of 12/31/94.
[b]Several hundred workers were still employed at the plant after 1988 when personnel records were collected.
[c]Cumulative employment figures based on total employment in the selected departments through 1988.

TABLE II. Selected Causes of Death by Exposure Group Among New York Rubber Manufacturing Workers

	Exposure groups											
	Definitely exposed				Possibly exposed				Probably not exposed			
Cause of death	Observed	Expected	SMR	95% CI	Observed	Expected	SMR	95% CI	Observed	Expected	SMR	95% CI
Cancer of biliary tract, liver, gall bladder	1	0.25	4.0	0.1, 22.5	0	0.23	0.0	—, 15.7	4	0.32	12.3[b]	3.4, 31.5
Lung cancer	7	5.15	1.4	0.5, 2.8	3	5.05	0.6	0.1, 1.7	3	6.7	0.4	0.1, 1.3
Prostate cancer	1	0.72	1.4	0.03, 7.6	0	0.92	0.0	—, 4.0	1	1.02	0.98	0.02, 5.5
Pancreatic cancer	0	0.69	0.0	—, 5.3	0	0.70	0.0	—, 5.2	3	0.94	3.2	0.66, 9.3
Kidney cancer	0	0.39	0.0	—, 9.4	1	0.36	2.7	0.07, 15.2	0	0.51	—	—, 7.2
Bladder cancer	1	0.26	3.8	0.1, 21.1	0	0.32	0.0	—, 11.3	1	0.39	2.6	0.07, 14.3
Brain cancer	1	0.61	1.6	0.04, 9.1	1	0.46	2.2	0.06, 12.2	0	0.76	0.0	—, 4.8
Cancer, unspecified sites	4	1.03	3.9[a]	1.05, 9.9	1	0.95	1.1	0.03, 5.8	0	1.33	0.0	—, 2.8
Lymphatic, hematopoetic cancers	2	1.71	1.2	0.14, 4.2	2	1.40	1.4	0.17, 5.15	3	2.17	1.4	0.3, 4.0
Benign and unspecified neoplasms	0	0.20	0.0	—, 18.0	0	0.18	0.0	—, 20.7	1	0.27	3.7	0.1, 20.8
All cancer deaths	17	14.96	1.1	0.66, 1.8	13	14.30	0.91	0.5, 1.6	19	19.93	0.95	0.6, 1.5
Disease of genitourinary system	0	0.62	0.0	—, 6.0	0	0.62	0.0	—, 5.9	2	0.86	2.3	0.3, 8.5
Ischemic heart disease	22	14.61	1.51	0.94, 2.3	17	16.88	1.01	0.6, 1.6	22	21.25	1.04	0.65, 1.57
All deaths	65	68.0	0.96	0.7, 1.2	47	59.2	0.8	0.6, 1.06	78	88.2	0.88	0.7, 1.1

[a] Two-sided Poisson, $P = 0.0423$.
[b] Two-sided Poisson, $P = 0.0007$.

(two identified as small cell carcinoma) with ''primary unknown''. Among workers in the group ''possibly exposed'' to the rubber chemicals, there were no deaths from bladder cancer, and no significant excesses in any cause-specific category of death. The group of workers never assigned to the rubber chemicals department was comprised mostly of workers who had been assigned to the polyvinyl chloride production department. This group had a statistically significant elevation in deaths from cancer of the biliary passages, liver, and gall bladder (SMR = 12.3; CI = 3.3–31.5). No other significant elevations in cause-specific mortality were observed in this group.

The risk of IHD mortality was further examined by stratifying on age, duration exposed (defined as duration employed in specific departments), time since first exposure, and calendar year (Table III). Elevated SMRs for IHD (SMR = 2.4; 95% CI = 1.1–4.7) were observed among ''definitely exposed'' workers younger than 50 years of age. Although based on small numbers, IHD mortality risk (SMR = 0.4; 95% CI = 0.01, 2.4) was lower for ''possibly exposed'' workers younger than 50 years of age. There was an excess risk of IHD death (SMR = 1.6; CI = 0.6–3.3) for the ''probably not exposed'' workers less than 50 years of age. An elevation in IHD mortality was observed among the ''definitely exposed'' workers with greater than 15 years since first exposure (SMR = 1.7; 95% CI = 1.0–2.8). The ''definitely exposed'' workers also had elevated death from IHD for the time period 1980–1994 (SMR = 1.7; 95% CI = 1.03–2.7) and with greater than 15 years of exposure to the rubber chemicals department (SMR = 2.3; CI = 0.6–5.9). SMRs based on county rates (Table IV) show similar trends but with lower SMRs.

Among the 143 workers whose smoking histories were obtained, 41 (28.7%) had never smoked, 62 (43.4%) were current smokers, and 40 (28.0%) were former smokers. Comparable smoking prevalence rates in the U.S. population, when directly standardized to the age distribution of the cohort, were 32.2% for those who had never smoked, 36.8% for current smokers, and 31.0% for former smokers. Thus, cohort members were slightly more likely to be current or former smokers than was the general U.S. population. The differences in smoking habits between the cohort and the U.S. population would account for an SMR of 1.03 for IHD.

IHD Mortality: Internal Cohort Comparisons

Internal comparisons were conducted by using multivariate Poisson regression models with a log-linear link

TABLE III. Risk of IHD Mortality (U.S. Rate Comparison) by Exposure Group, Age, Calendar Time, Time Since First Exposure, and Duration of Exposure Among New York Rubber Manufacturing Workers

	Exposure group								
	Definitely exposed			Possibly exposed			Probably unexposed		
	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
Age (years)									
< 50	9	3.69	2.4[a]	1	2.36	0.4	7	4.49	1.6
> 50	13	10.91	1.2	16	14.51	1.1	15	16.75	0.9
Calendar time									
< 1970	1	0.71	1.4	2	2.50	0.8	3	3.50	0.9
1970–79	3	3.46	0.9	2	4.87	0.4	7	5.43	1.3
1980–89	11	6.28	1.8	8	5.95	1.3	8	7.25	1.1
1990–94	7	4.11	1.7	5	3.55	1.4	4	5.06	0.8
Time since first exposure									
< 5 years	1	1.23	0.8	1	1.14	0.9	0	0.86	0
5–15 years	5	4.12	1.2	3	3.87	0.8	7	4.57	1.5
> 15 years	16	9.24	1.7[a]	13	11.87	1.1	15	15.82	0.9
Duration employed in department									
< 5 years	16	9.72	1.6	5	4.57	1.1	7	7.45	0.9
5–15 years	2	3.17	0.6	5	6.72	0.7	7	4.34	1.6
> 15 years	4	1.72	2.3	7	5.58	1.3	8	9.46	0.8

[a]For "Definitely exposed" workers, the following were statistically significant elevations in SMR for IHD. < 50 years: SMR = 2.5, (CI: 1.1–4.6) and > 15 years time since first exposure: SMR = 1.7 CI: 1.0–3.5).

TABLE IV. Risk of IHD Mortality by Exposure Group, Age, Calendar Time, Time Since First Exposure and Duration of Exposure Among New York Rubber Manufacturing Workers: Niagara County, NY Rate Comparison[a]

	Exposure group								
	Definitely exposed			Possibly exposed			Probably unexposed		
	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
Age (years)									
< 50	9	4.66	1.9	1	2.58	0.4	7	5.15	1.4
> 50	13	13.81	0.9	15	16.86	0.9	15	19.7	0.8
Calendar time									
< 1970	1	0.76	1.3	1	2.23	0.4	3	3.26	0.9
1970–79	3	3.88	0.8	2	5.21	0.4	7	5.98	1.2
1980–89	11	8.29	1.3	8	7.56	1.1	8	9.19	0.9
1990–94	7	5.54	1.3	5	4.44	1.1	4	6.45	0.6
Time since first exposure									
< 5 years	1	1.38	0.9	0	0.8833	0.0	0	0.85	0
5–15 years	5	5.01	1.0	3	4.07	0.7	7	5.34	1.3
> 15 years	16	12.08	1.3	13	14.57	0.9	15	18.69	0.8
Duration employed in department									
< 5 years	16	12.34	1.3	4	5.03	0.8	7	7.84	0.9
5–15 years	2	3.98	0.6	5	6.69	0.8	7	4.73	1.5
> 15 years	4	2.15	1.9	7	7.75	0.90	8	12.30	0.7

[a]One death occurring before 1960 was dropped from this analysis for the "possibly exposed" group because rate files for Niagara County, NY begin in 1960.

function. Internal comparisons were made for the "definitely exposed" group versus the two other groups individually and combined. Parallel analyses were also conducted with the two groups as separate reference populations (not presented). To evaluate whether a variable was an important predictor of ischemic heart disease risk, a series of nested models was fit and likelihood ratio tests were used to identify which parameters significantly improved the fit of the model to the data. Further evaluation of the effects of age and exposure group was done by fitting models with more than two age categories. In addition to age (< 50 and 50+), the following variables were also examined in the models: (i) exposure group ("exposed" versus reference group); (ii) time since first exposure (20+ years relative to < 20 years); (iii) duration exposed (20+ years relative to < 20 years), and (iv) interaction terms between age (dichotomous groupings) and exposure group. This analysis found that IHD risk was positively associated with age and not significantly associated with exposure group or any other exposure variable. Use of more refined age strata did not substantially alter the results (i.e., IHD risk increased monotonically with age and exposure group was not significant). However, it was noted that for analyses using dichotomous age categories, the cutpoint at age 45 gave the lowest *P*-value for exposure status. To examine differential risk of IHD by exposure group, an interaction term between age (< 45 vs. 45+ years) and exposure category was fit. Although the interaction term was not statistically significant ($P = 0.12$), there was a positive association of IHD with exposure among workers under 45 years of age (SRR = 2.9, 95% CI: 1.3, 11.5), which is consistent with the observations from the SMR analysis.

The addition of time since first exposure and duration to models with main effects for exposure group and age indicated that these variables were not significantly associated with IHD mortality. As compared to workers with less than 20 years since first exposure, workers with 20 or more years since first exposure had a 1.4-fold greater risk of IHD mortality (95% CI = 0.7–2.7, $P = 0.3$). For duration employed in specified departments, workers employed for less than 20 years had a 1.3-fold excess risk of IHD relative to workers employed for greater than 20 years (95% CI = 0.7–2.3, $P = 0.4$). The SRR for IHD among "definitely exposed" workers compared to the internal reference group (combined lower exposed groups) was 1.03 (CI = 0.6–1.7). Separate comparison of the "definitely exposed" group to the "probably not exposed" group and to the "possibly exposed" group showed results similar to those from analyses with the combined reference population.

DISCUSSION

This mortality study found that IHD mortality among workers in the rubber chemicals department was elevated

relative to IHD mortality in the U.S. population; some of this excess may be related to higher rates of IHD mortality in the county where the plant is located. Depending on which referent rates were used, SMRs for IHD among workers in the rubber chemicals department ranged from 1.2 to 1.5, with SMRs in the under 50 age group ranging from 1.9–2.5. Workers under 50 in the ''probably unexposed'' group also had elevated (but not statistically significant) SMRs for IHD (SMRs ranging from 1.4–1.6). Poisson regression analyses did not show a significant effect of exposure group or a significant interaction between exposure and age. This may be attributed to the fact that the internal reference population is not truly unexposed with respect to chemical exposure nor to job parameters related to rotating shift schedules. This, in combination with a sparseness of deaths, would reduce the power to detect an effect if one existed.

An important consideration in interpreting IHD mortality in occupational cohort studies is the healthy worker effect. The healthy worker effect refers to the observation that ''all cause'' mortality of occupational groups is generally lower than that of the general population, because the occupational groups includes persons who are healthy enough to obtain and hold employment, while the general population includes many persons who do not seek employment for reasons of health [Sterling and Weinkam, 1986]. Deaths from heart disease tend to track with ''all cause'' mortality in the absence of a strong occupational effect, because heart disease deaths are such a large proportion (approximately 50%) of total deaths. Thus, in an analysis of the healthy worker effect by using mortality data from ten occupational cohort studies, Monson [1986] found that SMRs for circulatory diseases ranged from 0.6 to 1.2, with 7 of the 10 cohorts having SMRs below 1.0. In another analysis of the healthy worker effect, Sterling and Weinkam [1986] examined mortality among U.S. veterans who were selected for study because they have health status comparable to that of persons able to seek employment; the SMR for heart disease was 0.67 for persons aged 35–54 and 0.75 for persons aged 55–84. There is no agreed upon method to adjust for the healthy worker effect [Choi, 1992]. Much of the data on the healthy worker effect stems from studies of mortality in the 1950s through 1970s, while data suggest increasing socioeconomic differentials in IHD mortality in recent decades [Wing et al., 1987]. The potential impact of these changes on the magnitude of the healthy worker effect in occupational cohorts studied in recent decades has not been examined. However, in this study the use of county referent rates may partly address the health worker effect, as coronary heart disease mortality by county in the U.S. is highly associated with county occupational structure [Armstrong et al., 1998].

Although the conclusions of our study are limited by the small sample size and difficulties in defining an appropriate referent population, we view the results as suggestive of an occupationally related increased risk for IHD, particularly among workers under 50. One potential risk factor for IHD mortality that affects both the rubber chemicals and polyvinyl chloride departments, but not maintenance and shipping, is the rotating shift schedule required for personnel assigned to these units. Two prior studies have found an increase in coronary heart disease incidence among rotating shift workers. Knuttson et al. [1986] found a nonsignificant relative risk (RR) of 1.4 for incident IHD among rotating workers compared to day workers at a pulp and paper plant; the RR was 2.2 ($P = 0.04$) for workers with 11–15 years of shiftwork. Kawachi et al. [1995] examined incident CHD in a large cohort of U.S. female nurses, and found that those who worked rotating night shifts had an age-adjusted RR of CHD of 1.38 (C.I. 1.08–1.76); the RR was 1.51 (C.I. = 1.12–2.03) among those reporting six or more years of rotating night shifts. The shift rotation pattern for workers in both the rubber chemicals and polyvinyl chloride departments may involve greater physiologic disruption than alternative patterns. Workers in these units changed shifts about once a week in a pattern that rotated backward, with some shift trading (people working two shifts in a row). Backward shift rotation has been associated with physiological disruptions [Moore-Ede and Richardson, 1985], including some risk factors for cardiovascular disease such as serum triglyceride levels and systolic blood pressure [Knutsson et al., 1988; Orth-Gomer, 1983].

A potential cardiovascular risk factor that affects the rubber chemicals department is exposure to CS_2. CS_2 has been associated with elevated IHD mortality in a number of studies of workers in the viscose rayon industry [McMahon and Monson, 1988; Nurminen and Hernberg, 1985]; limited data suggest that CS_2 exposures <10 ppm are not associated with elevated IHD mortality [Nurminen and Hernberg, 1985]. A proportional mortality study by Liss and Finkelstein [1996] found no association of IHD with CS_2 exposures ranging from 1 to 20.8 ppm. Cardiovascular effects have been associated with mean 8-hour time weighted average (TWA) exposures to CS_2 in the ranges of 4.1–11.8 ppm [Egeland et al., 1992] and of 2.6–47.4 ppm [Swaen et al., 1994]. A Dutch cohort mortality study [Swaen et al., 1994] of 3322 workers from a viscose textile plant reported an excess risk of IHD of 1.15 but a negative dose–response relationship with CS_2 exposure levels. Similarly, a cross-sectional study of CHD risk factors (i.e., blood pressure, high-density lipoproteins) among viscose industry workers in Germany [Drexler et al., 1995] found an inverse relationship with cumulative CS_2 exposure. These authors noted that all subjects had done shift work, which may account for the observed negative relationship with the CHD risk factors studied. CS_2 exposures, determined by personal

air sampling, ranged from < 0.2 ppm to 65.7 ppm for this study.

A previous study evaluated CS_2 exposure, cardiovascular disease risk factors and symptoms at the study plant [Oliver and Weber, 1984]. Based on 8-hour TWAs, the investigators reported maximum exposures of 0.67 ppm CS_2, substantially below levels of exposure associated with IHD risk in the viscose rayon industry. The morbidity study included 89 workers in the rubber chemicals department (exposed group) and 65 reference workers from outside the department. There were no significant differences between the exposed and referent groups with respect to cardiovascular disease risk factors, including serum cholesterol, hypertension, and weight. However, exposed workers were more likely than referents to report chest pain (50.6% vs. 20%, $P < 0.05$) and to be classified as having definite or possible angina (26.4% vs. 7.6%, $P < 0.05$), an association which retained its statistical significance after controlling for age and cigarette smoking. Mean urinary aromatic amine and blood methemoglobin levels were higher in the exposed group than in the references, and were slightly higher (but not statistically significant) among workers with chest pain and angina compared to those without. There are no data concerning IHD risk in populations with chronic methemoglobinemia or potential synergism between the effects of CS_2 exposure and methemoglobinemia.

Increased mortality from IHD is present during the most recent time periods analyzed (1985–1989 and 1990–1994) in the SMR analysis. Hence, intervention to reduce exposure to occupational risk factors for IHD may be warranted. NIOSH investigators recommended that the labor-management health and safety committee evaluate the extent to which such risk factors currently exist in the plant. If the plant continues to use a backward rotating shift schedule, modifications should be considered [Knauth, 1997]. NIOSH has previously made recommendations [NIOSH, 1989] to reduce aromatic amine exposures in the rubber chemicals department and recommends that current levels of exposure to aromatic amines and CS_2 be evaluated. It was also recommended that the labor-management health and safety committee consider whether current workers might benefit from a plant-based intervention program to monitor and reduce cardiovascular risk factors.

With regard to other causes of death, the only cause that was significantly elevated was cancer of the biliary tract, liver, and gallbladder among workers never assigned to the rubber chemicals department, which was consistent with a previous study of polyvinyl chloride production workers at this facility [Nicholson et al., 1975]. Bladder cancer was not elevated, despite the known excess in incident cases. This confirms previous observations that studying mortality for cancers that have a high survival rate may lead to spuriously negative findings [Axtell et al., 1998].

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