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Cancer Mortality and Wood Dust Exposure Among Participants in the American Cancer Society Cancer Prevention Study-II (CPS-II)

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In 1994, the International Agency for Research on Cancer (IARC) classified wood dust as a human carcinogen, based on very strong evidence of a carcinogenic risk of sino-nasal cancer. Excesses of other cancers, including lung and stomach, have been reported among persons employed in wood industries or occupationally exposed to wood dust, but not as consistently. We investigated such possible associations using the mortality experience of 362,823 men enrolled in the American Cancer Society's Cancer Prevention Study — II in 1982 and followed up for 6 years. Within this group, 45,399 men (12.5%) reported either employment in a wood-related occupation or exposure to wood dust or both. Among woodworkers, a small but significant excess risk was found for all causes of death (RR 1.17 (95% CI 1.11–1.24)) and for total malignancies (RR 1.17 (1.05–1.30)). Among men who reported exposure to wood dust, there was an elevated risk of total mortality (RR 1.07 (1.03–1.11)), total malignancies (RR 1.08 (1.01—1.15)), and lung cancer (RR 1.17 (1.04–1.31)). Among woodworkers, a significant trend (P = 0.02) of increasing risk of lung cancer with increasing duration of exposure was observed. An unexpected, significantly increased mortality from prostate cancer was observed in both wood-employed and wood-exposed, and a twofold increased risk of fatal brain cancer was seen among the former. Lung cancer mortality was especially high among woodworkers who also reported exposure to asbestos or formaldehyde, and it appears that exposure to these known carcinogens may partly explain the observed increased risks. Excess sino-nasal cancer was not observed, but the number of cases was small. Am. J. Ind. Med. 34:229–237, 1998. © *1998 Wiley-Liss, Inc.*

KEY WORDS: respiratory disease; occupational diseases; woodworkers; wood dust; asbestos; formaldehyde

INTRODUCTION

In 1994, the International Agency for Research on Cancer [IARC, 1995] classified wood dust as a human carcinogen, based on very strong evidence of a carcinogenic risk of sino-nasal cancer. Excesses of other respiratory, digestive, lymphatic, and hematopoietic neoplasms associated with exposure to wood dust or a history of employment in wood-related occupations have been observed in epidemiological studies, but the evidence has been mixed. For example, Siemiatycki and colleagues [1986] observed excesses of lung, stomach, and, possibly, colorectal cancer among residents of Montreal with ''substantial'' exposure to

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wood dust for 15 or more years. Vaughan and Davis [1991] observed an excess of cancer at various upper respiratory sites in residents of western Washington State who had been employed in wood dust-exposed jobs for 10 or more years. After allowing for a 15-year latency, the relative risks observed were highest for sino-nasal cancer, but excess risks were also observed for nasopharyngeal, other pharyngeal, and laryngeal cancers. Stellman and Garfinkel [1984] observed an excess of stomach cancer and a small excess of lung cancer among woodworkers in a prospective analysis of mortality among participants in an American Cancer Society survey. However, the results of studies of woodworkers for respiratory (other than the nasal sinuses), digestive, and lymphatic and hematopoietic cancers have been far from consistent. For example, among the British furniture workers cohort [Acheson et al., 1984; Demers et al., 1995], a cohort known to have had high exposures to wood dust, only excesses of sino-nasal and nasopharyngeal cancer have been observed.

Any excess relative risks for these other sites are likely to be moderate in comparison with sino-nasal cancer, but even a small excess of a common site may be of greater public health significance than a large excess of sino-nasal cancer. There have been relatively few cohort studies of woodworkers and many are subject to a variety of problems such as low power to detect small excess risks, lack of appropriate controls to neutralize the ''healthy worker effect,'' and unavailability of data on confounding factors such as smoking and other occupational exposures. The American Cancer Society's Cancer Prevention Study II (CPS-II) included questions to enrolled subjects regarding occupational history, exposure to wood dust, and smoking history. This presented us with the opportunity to examine the relationship between wood dust and employment as a woodworker and the subsequent risk of developing common cancers using a useful dataset which included an internal comparison population and information on potentially confounding factors.

METHODS

The subjects in this study were selected among those enrolled in CPS-II, details of which have been previously reported [Stellman and Garfinkel, 1986; Stellman et al., 1988].

To summarize, in 1982 more than 77,000 volunteer ''researchers'' enrolled 509,000 men and 677,000 women in all 50 states, the District of Columbia, and Puerto Rico. The subjects completed a four-page confidential questionnaire on history of cancer and other diseases; body weight and height; exercise; occupations and occupational exposures; and personal habits such as drinking, smoking, and diet. Enrollment was in family groups, with at least one person above the age of 45 in each family. All family members 30 years or older were asked to complete a questionnaire.

Every second year, the volunteer ''researchers'' were given lists of persons whom they had enrolled and asked to check whether they were alive or dead, and if dead, the date and place of death. Copies of death certificates were obtained from state health departments and coded to the 9th revision of the International Classification of Diseases (ICD-9). For about one-quarter of reported cancer deaths, inquiry was made through cancer registries, physicians, or hospitals to verify the primary site of diagnosis. The present analysis is restricted to male subjects who were traced for up to 6 years; for this group, follow-up was 98% complete.

Details of occupational assignment have been reported previously [Stellman et al., 1988]. Occupations and exposures were determined independently. Occupation was ascertained via a combination of three questions: current occupation, last occupation if retired, and occupation held for the longest period of time. Exposure was reported via a check-off list of 12 distinct hazards that included, among others, asbestos, coal tar pitch or asphalt, coal or stone dust, formaldehyde, and ionizing radiation.

For this study, two partially overlapping exposed groups were identified: 1) woodworkers, and 2) wood dust-exposed men. The woodworkers were defined as men who reported a wood-related occupation (carpenter; lumber worker; furniture maker, repairer, or finisher; logger; sawmill operative; woodworker; or woodcutter) as their current, last, or longest held job. The wood dust-exposed men were those who reported ''regular'' exposure to wood dust in the exposure history matrix. The comparison group consisted of persons who did not report previous employment in a wood-related job and who replied ''no'' to the wood dust exposure question.

The risk of death due to cancer among each of the two exposed groups, as defined above, was calculated with respect to the unexposed reference population. In addition, since asbestos and formaldehyde are two exposures that are commonly reported among woodworkers, the risk of cancer among woodworkers who also reported exposure to either of these two substances was explored. An individual was considered at risk from the date of enrollment (September, 1982, for the great majority) through date of death or end of follow-up (August, 1988). Men with missing vital status were excluded from the analysis.

Incidence density ratios were used to estimate relative risks (RR) and were calculated using maximum likelihood methods [Breslow and Day, 1987]. Approximate 95% confidence intervals (CI), based on the standard error of the coefficients, were derived from the Poisson regression model. Poisson regression modeling was also used to analyze the relation between cancer risk and duration of wood dust exposure. Detailed analyses were only performed for sites with at least ten observed cancers among either the woodworkers or the wood dust-exposed men. Adjustment

TABLE I. Persons, Person-Years, and Deaths Among Study Groups; American Cancer Society Cancer Prevention Study II

Study group	Persons	Person-years	Total deaths	Cancer deaths
Any wood occupation or exposure	45,399	261,871	3,697	1,158
Wood dust exposure only	33,858	196,384	2,426	777
Wood occupation only	5,222	29,289	702	197
Both wood exposure and occupation	6,319	36,198	569	184
Wood occupation with or without exposure: ''woodworkers''	11,541	65,487	1,271	381
No wood exposure or occupation	317,424	1,839,274	22,994	7,203
Total	362,823	2,101,145	26,691	8,361

for age and smoking status was performed using five age groups (30–49, 50–59, 60–69, 70–79, 80+) and four smoking categories (never, past, current, missing). Adjustment for age and smoking using more detailed classifications did not alter the estimates appreciably. All variables were treated in a categorical fashion except when calculating trends for duration of wood dust exposure. Poisson regression analyses were performed using EGRET statistical software (Statistics and Epidemiology Research, Seattle, WA).

The analysis focused on cancer sites considered to be of a priori suspicion because they have been observed in excess among workers in wood-related or wood dust-exposed jobs in at least two well-conducted studies. The sites chosen were the nasopharyngeal [Demers et al., 1995; Kawachi et al., 1989; Vaughan and Davis, 1991], laryngeal [Maier et al., 1992; Vaughan and Davis, 1991], lung [Esping and Axelson, 1980; Kawachi et al., 1989; Siemiatycki et al., 1986; Stellman and Garfinkel, 1984], stomach [Olsen et al., 1988; Siemiatycki et al., 1986; Stellman and Garfinkel, 1984], and colorectal cancers [Peters et al., 1989; Siemiatycki et al., 1986; Swanson and Belle, 1982; Swanson et al., 1985; Tilley et al., 1990] as well as Hodgkin's lymphoma [Partanen et al., 1993; Persson et al., 1993], non-Hodgkin's lymphoma [Partanen et al., 1993; Persson et al., 1993], multiple myeloma [Demers et al., 1995; Flodin et al., 1987], and leukemia [Burkhart, 1982; Flodin et al., 1987]. These sites were also those chosen for detailed review in the IARC monograph [1995] on wood dust. Risks for non-malignant respiratory diseases among woodworkers in this cohort are presented in a separate report [Demers et al., 1998].

RESULTS

From the original CPS-II cohort of over half a million men, a total of 362,823 had sufficient data to be included in an analysis of cancer risk (Table I). Of these, 45,399 (12.5%) reported either employment in a wood-related occupation or exposure to wood dust, accounting for over one-quarter million person-years. There were 1,158 cancer deaths reported in this group during the 6-year follow-up period (Table I). A total of 6,319 (55%) of all those employed in wood-related occupations (''woodworkers'') reported being regularly exposed to wood dust, 1,480 (13%) reported exposure to asbestos, and 387 (3%) reported exposure to formaldehyde. There was some overlap in reported exposures; 1,194 woodworkers (10%) reported both wood dust and asbestos exposure, 305 (3%) reported both wood dust and formaldehyde exposure, and 151 (1.3%) reported all three exposures (wood dust, asbestos, and formaldehyde). The most common jobs reported by participants who reported exposure to wood dust but not employment in a wood-related occupation were managers (17%), teachers (9%), sales (9%), farming (9%), and construction (7%).

Table II presents the results for all major cancer sites both for men who had been employed in a wood-related occupation (woodworkers) and for men who reported being regularly exposed to wood dust. As previously noted, these two groups are not mutually exclusive. A small, statistically significant excess of deaths from all causes combined and for total cancers was observed in both groups. There were no causes of death with significantly reduced risks. Among the a priori suspected cancers, a small excess was observed for lung cancer among both the wood dust-exposed men and the woodworkers, while a nonsignificant excess was seen for stomach cancer among the wood dust-exposed men only. Excesses based on small numbers of deaths were observed for rectal cancer among both groups, and for laryngeal cancer among wood dust-exposed men. In addition, excess risks were observed for two cancer sites that were not of a priori interest: increased prostate cancer was observed among wood dust-exposed men (RR = 1.2) and woodworkers (RR = 1.5), and an excess of brain cancer was observed among woodworkers (RR = 2.0). Excesses based on very small numbers of deaths were observed for both pleural neoplasms (RR = 2.5) and soft tissue sarcomas (RR = 2.5) among the woodworkers.

TABLE II. Risk of Death Among Men by Wood Dust Exposure and Occupation Group*

	Wood dust exposure			Wood-related occupation			Reference
Cause of death (ICD9)	**Observed**	**RR**	**(95% CI)**	**Observed**	**RR**	**(95% CI)**	**Observed**
All causes of death	2,995	1.07	(1.03–1.11)	1,271	1.17	(1.11–1.24)	22,994
All malignant neoplasms (140–208)	961	1.08	(1.01–1.15)	381	1.17	(1.05–1.30)	7,203
Oral cancer (140–145)	9	1.06	(0.53–2.13)	1	0.33	(0.05–2.35)	68
Pharyngeal cancer (146–149)	7	0.92	(0.42–2.03)	2	0.82	(0.21–3.38)	59
Nasopharyngeal cancer (147)	1	0.44	(0.06–3.29)	1	1.44	(0.19–10.9)	18
Esophageal cancer (150)	28	1.31	(0.88–1.95)	6	0.81	(0.36–1.83)	171
Stomach cancer (151)	40	1.34	(0.96–1.87)	11	1.05	(0.57–1.92)	241
Colon cancer (153)	100	1.04	(0.84–1.28)	37	1.04	(0.75–1.45)	788
Rectal cancer (154)	23	1.31	(0.84–2.04)	9	1.47	(0.75–2.89)	142
Liver cancer (155)	10	0.61	(0.32–1.56)	2	0.34	(0.08–1.39)	132
Pancreatic cancer (157)	47	0.90	(0.66–1.21)	23	1.19	(0.78–1.82)	425
Sino-nasal cancer (160)	1	1.05	(0.13–8.39)	0	0.00		8
Laryngeal cancer (161)	8	1.60	(0.75–3.43)	2	1.19	(0.29–4.94)	40
Lung cancer (162)	317	1.17	(1.04–1.31)	111	1.14	(0.94–1.37)	2,158
Pleural neoplasms (163)	3	1.43	(0.42–4.87)	2	2.51	(0.57–10.9)	17
Soft tissue sarcoma (171)	5	0.80	(0.32–2.00)	5	2.45	(0.97–6.17)	50
Malignant melanoma (172)	13	0.69	(0.39–1.22)	5	0.85	(0.35–2.08)	151
Prostate cancer (185)	110	1.23	(1.00–1.50)	59	1.49	(1.14–1.95)	754
Bladder cancer (188)	24	0.99	(0.65–1.51)	14	1.41	(0.82–2.43)	201
Kidney cancer (189)	24	0.84	(0.55–1.28)	7	0.74	(0.35–1.57)	230
Brain tumors (191)	32	1.14	(0.78–1.64)	18	2.02	(1.25–3.27)	227
Lymphatic & hematopoietic neoplasms							
Total (200–208)	91	1.01	(0.81–1.26)	31	0.97	(0.68–1.40)	726
Non-hodgkin's lymphoma (200, 202)	39	1.09	(0.78–1.52)	12	0.97	(0.55–1.73)	289
Hodgkin's lymphoma (201)	4	1.20	(0.42–3.44)	1	1.04	(0.14–7.68)	26
Multiple myeloma (203)	16	1.04	(0.62–1.76)	4	0.72	(0.26–1.94)	124
Leukemia (204–208)	32	0.90	(0.63–1.30)	14	1.08	(0.63–1.85)	287

*Adjusted for age and smoking status (never/past/current/missing). All comparisons are relative to participants who did not report either employment in a wood occupation or regular exposure to wood dust.

Table III presents the results for the cancer sites of a priori suspicion which had at least 10 deaths among either the woodworkers or wood dust-exposed men. Results are presented for three mutually exclusive groups: 1) men who reported wood dust exposure but had not been employed in a wood-related job; 2) men who had been employed in a wood-related occupation but did not report wood dust exposure; and 3) men who had both been employed in a wood-related occupation and reported wood dust exposure.

Deaths from all causes combined were elevated in all three groups by up to 18%, and for total cancer were elevated by 20% in the latter group. Excesses of lung cancer were observed among woodworkers who reported regular wood dust exposure and among men reporting wood dust exposure who were not woodworkers. An excess of stomach cancer was observed only among non-woodworkers reporting exposure to wood dust. The highest rectal cancer risk was observed among woodworkers who reported regular wood dust exposure (based on five deaths).

Adjustment for self-reported exposure to asbestos or formaldehyde had little effect on the estimates of lung cancer risk presented in Table III, although precision was somewhat decreased because of collinearity of exposure. For example, the RR of lung cancer among men who had been employed in a wood-related occupation and who also reported wood dust exposure was 1.27 (95% CI = 0.94–1.72) after adjustment for asbestos exposure and 1.22 (95% CI = 0.87–1.70) after adjustment for formaldehyde exposure. Adjustment for these collateral exposures also slightly reduced the RR of stomach and rectal cancer. The association between wood dust exposure and wood-related occupations and rectal cancer disappeared after adjustment either for exposure to asbestos or formaldehyde. Much of the apparent loss of effect for stomach and rectal cancers

TABLE III. Risk of Death Among Men by Wood Dust Exposure and Occupation Group*

	Wood dust exposure only		Wood-related occupation only		Exposure and occupation	
Cause of death	**Observed**	**RR (95% CI)**	**Observed**	**RR (95% CI)**	**Observed**	**RR (95% CI)**
All causes	2,426	1.05 (1.00–1.09)	702	1.18 (1.10–1.27)	569	1.16 (1.07–1.26)
All cancers	777	1.05 (0.98–1.13)	197	1.14 (0.99–1.32)	184	1.20 (1.03–1.39)
Stomach cancer	35	1.41 (0.99–2.01)	6	1.07 (0.48–2.42)	5	0.98 (0.40–2.38)
Colon cancer	83	1.04 (0.83–1.31)	20	1.06 (0.68–1.65)	17	1.03 (0.64–1.67)
Rectal cancer	18	1.24 (0.76–2.02)	4	1.25 (0.46–3.38)	5	1.67 (0.68–4.07)
Lung cancer	258	1.15 (1.01–1.31)	52	1.03 (0.78–1.36)	59	1.25 (0.97–1.62)
All lymphatic/hematopoietic	74	0.99 (0.78–1.26)	14	0.84 (0.49–1.42)	17	1.12 (0.69–1.81)
Non-Hodgkin's lymphoma	33	1.11 (0.78–1.59)	6	0.94 (0.42–2.11)	6	1.00 (0.45–2.25)
Multiple myeloma	14	1.11 (0.64–1.92)	2	0.67 (0.17–2.72)	2	0.76 (0.19–3.06)
Leukemia	23	0.78 (0.51–1.20)	5	0.72 (0.30–1.76)	9	1.48 (0.76–2.88)

*Adjusted for age and smoking status. All comparisons are relative to participants who did not report either employment in a wood occupation or regular exposure to wood dust.

TABLE IV. Risk of Death Among Men by Duration (Years) of Wood Dust Exposure*

	Less than 10 yr		10 to 19 yr		20 or more yr	
Cause of death (*P*-value, trend)	**Observed**	**RR (95% CI)**	**Observed**	**RR (95% CI)**	**Observed**	**RR (95% CI)**
All cause ($P = 0.006$)	745	0.97 (0.90–1.04)	483	1.04 (0.95–1.14)	1,122	1.10 (1.04–1.17)
All cancer ($P = 0.06$)	239	0.97 (0.85–1.10)	161	1.09 (0.93–1.27)	358	1.10 (0.99–1.23)
Stomach cancer ($P = 0.37$)	12	1.44 (0.80–2.58)	10	2.02 (1.07–3.80)	10	0.93 (0.49–1.74)
Colon cancer ($P = 0.61$)	22	0.82 (0.54–1.26)	17	1.06 (0.66–1.72)	39	1.12 (0.81–1.55)
Rectal cancer ($P = 0.43$)	5	1.03 (0.42–2.51)	4	1.38 (0.51–3.73)	8	1.25 (0.61–2.55)
Lung cancer ($P = 0.03$)	77	1.03 (0.82–1.29)	59	1.31 (1.01–1.70)	115	1.16 (0.96–1.40)
All lymphatic/hematopoietic ($P = 0.63$)	20	0.79 (0.51–1.24)	18	1.20 (0.75–1.91)	35	1.09 (0.77–1.53)
Non-Hodgkin's lymphoma ($P = 0.36$)	11	1.08 (0.59–1.97)	8	1.33 (0.66–2.68)	15	1.18 (0.70–1.99)
Multiple myeloma ($P = 0.33$)	2	0.48 (0.12–1.92)	4	1.58 (0.59–4.29)	8	1.42 (0.70–2.91)
Leukemia ($P = 0.36$)	5	0.51 (0.21–1.23)	5	0.85 (0.35–2.06)	11	0.86 (0.47–1.57)

*Adjusted for age and smoking status. Includes all wood-exposed persons regardless of occupation. Persons who reported a wood-related occupation but no wood exposure were excluded from the analysis. All comparisons are relative to participants who did not report either employment in a wood occupation or regular exposure to wood dust.

appears to be due to the small numbers of subjects reporting wood dust exposure or employment in a wood-related occupation remaining in the models after excluding persons with missing formaldehyde or asbestos exposure information.

Table IV presents cancer risks by duration of wood dust exposure among both those who did and did not report employment in wood-related occupations. No clear associations with duration of wood dust exposure were apparent. Although the point estimates of risk did not increase monotonically, there was a significant trend for lung cancer ($P = 0.03$). When the duration of wood dust exposure was examined only among the woodworkers, a sharper association with lung cancer was observed (trend $P = 0.02$, RR = 0.70 (95% CI = 0.26–1.88) for less than 10 years, RR = 1.25 (95% CI = 0.62–2.50) for 10 to 19 years, and RR = 1.45 (95% CI = 1.07–1.96) for 20 or more years). No other statistically significant trends for other cancer sites were observed, nor was there a monotonic increase in risk, but the small numbers of deaths within the individual duration categories precluded examination of all but the most common cancer sites.

Risk estimates for possible effects of exposure to asbestos and formaldehyde are shown in Table V. Results are reported for non-woodworkers (men not employed in a wood-related job) who said they were exposed to asbestos, and for woodworkers exposed to asbestos; corresponding data for formaldehyde are also shown. An excess of all cancers combined was observed among woodworkers exposed to asbestos, primarily due to an excess of lung cancer.

TABLE V. Risk of Death Among Men by Asbestos and Formaldyde Exposure and Wood-Related Occupation*

	Asbestos exposure only		Asbestos exposure and occupation		Formaldehyde exposure only		Formaldehyde exposure and occupation	
Cause of death	Observed	RR (95% CI)	Observed	RR (95% CI)	Observed	RR (95% CI)	Observed	RR (95% CI)
All causes	1,127	1.07 (1.01–1.13)	144	1.28 (1.09–1.51)	1,238	1.02 (0.95–1.10)	33	1.20 (0.85–1.68)
All cancers	324	1.12 (1.01–1.23)	57	1.60 (1.23–2.07)	367	0.98 (0.86–1.12)	14	1.61 (0.95–2.72)
Stomach cancer	10	1.55 (0.99–2.42)	1	0.84 (0.12–5.96)	11	1.63 (0.94–2.86)	0	0.00
Colon cancer	35	1.00 (0.74–1.36)	2	0.52 (0.13–2.09)	37	1.00 (0.74–1.36)	0	0.00
Rectal cancer	7	1.40 (0.76–2.59)	2	2.92 (0.72–11.8)	8	0.21 (0.01–1.49)	1	5.77 (0.81–41.22)
Lung cancer	86	1.17 (0.99–1.38)	25	2.25 (1.52–3.33)	104	0.93 (0.73–1.18)	7	2.63 (1.25–5.51)
All lymphatic/hematopoietic	25	0.99 (0.72–1.51)	6	1.69 (0.75–3.77)	28	1.22 (0.84–1.77)	3	3.44 (1.11–10.68)
Non-Hodgkin's lymphoma	9	1.43 (0.93–2.18)	3	2.17 (0.70–6.78)	11	0.92 (0.50–1.68)	1	2.88 (0.40–20.50)
Multiple myeloma	3	1.34 (0.68–2.65)	1	1.67 (0.23–11.9)	4	0.74 (0.27–2.02)	0	0.00
Leukemia	12	0.31 (0.13–0.75)	2	1.38 (0.34–5.56)	12	0.96 (0.54–1.71)	2	5.79 (1.44–23.25)

*Adjusted for age and smoking status. All comparisons are relative to participants who did not report either employment in a wood occupation or regular exposure to wood dust.

Excesses of rectal cancer and of lymphatic and hematopoietic neoplasms were also observed among woodworkers exposed to asbestos. Exposure to asbestos was associated with lung and stomach cancer in non-woodworkers, although excesses based on smaller numbers were observed for rectal cancer and non-Hodgkin's lymphoma. When data for formaldehyde and employment in wood-related occupations were analyzed in a similar manner, an excess of all cancers was also observed among formaldehyde-exposed woodworkers, as were site-specific excesses of lung, rectal, and lymphatic and hematopoietic cancers. Only stomach cancer was associated with formaldehyde exposure in non-woodworkers. It should be noted that small numbers of exposed subjects precluded analyses of the formaldehyde data in further detail.

DISCUSSION

In this analysis, we did not observe any evidence of an excess sino-nasal cancer, the site most strongly associated with wood dust exposure [IARC, 1995]. Very high relative risks for sino-nasal cancer have been observed in many studies to be associated with high exposures and long latency. Excess risks observed in North American studies have generally been in the range of 2 to 5, much lower than those observed in European studies [Demers et al., 1995]. The absence of an effect in this study may be due to the relatively short follow-up period or exposures that were lower than those in other studies. Similarly, there was no association with nasopharyngeal cancer, a neoplasm that has also been associated, although less consistently than sino-nasal cancer, with wood dust exposure [IARC, 1995]. Both sino-nasal and nasopharyngeal cancers are quite rare in the United States [Burt et al., 1992; Nam et al., 1992] and among the 45,399 CPS-II participants who reported either a wood-related occupation or regular wood dust exposure, one and two cases, respectively, were observed.

In this study, we observed a small excess of lung cancer associated with wood dust exposure both within and outside of wood-related occupations. No excess was observed among woodworkers who did not report ''regular'' exposure to wood dust. The excess appears to be related to duration of exposure, but only a modest increase was observed even in the longest duration category. These results are consistent with the analysis of data of a similar previous ACS study, CPS-I [Stellman and Garfinkel, 1984]. Analyses of industry-based studies have generally found no excess of lung cancer [Demers et al., 1995; IARC, 1995; Kauppinen et al., 1993], even among workers who were highly exposed to wood dust such as the British furniture workers. However, excesses have been observed in some community-based case-control studies [Kawachi et al., 1989; Siemiatycki et al., 1986].

Excesses of lung cancer were also observed among woodworkers reporting exposure to asbestos or formaldehyde. The excess associated with asbestos exposure is not surprising, given the well-established association. Although based on small numbers, the excess of pleural cancer observed among woodworkers is also consistent with asbestos exposure.

Formaldehyde is an established animal carcinogen and, although a few studies have observed a small excess of lung cancer associated with formaldehyde exposure [Gerin et al., 1989; Gardner et al., 1993], this has not been confirmed in most available investigations [Andersen et al., 1982; Bond et al., 1986; Blair et al., 1987; Stayner et al., 1988; Bertazzi et al., 1989; Partanen et al., 1990; Andjelkovic et al., 1995]. A clear association between formaldehyde exposure and lung cancer in humans has not been established [IARC, 1995].

In experimental animals, formaldehyde is mainly absorbed in the upper respiratory tract [Heck et al., 1983; Casanova et al., 1991], and this is likely to be the case in humans [Risby et al., 1990; Rothenberg et al., 1989]. A transient, reversible decline in lung function without, however, chronic effects has been observed in several studies among workers exposed to formaldehyde with or without concomitant exposure to wood dust [IARC, 1995]. In particular, it has been proposed that adsorption of formaldehyde on the wood dust allows it to be carried deeper into the respiratory system [Jakab et al., 1992]. Blair and colleagues [1990] observed an increased risk of lung cancer among workers employed in jobs where exposure to formaldehyde occurred in combination with dust, including plywood workers.

The effect of exposures other than wood dust and formaldehyde and, in particular, tobacco smoking and asbestos among woodworkers may, in part, explain some of the inconsistency in the results of the studies of woodworkers. In our data, self-reported asbestos exposure was only a partial explanation of the excess risk of lung cancer. When the analysis was restricted to subjects with information on both asbestos and wood dust, the RR of lung cancer among non-woodworkers with self-reported wood dust exposure was 1.15 (95% CI 0.97–1.33) before adjustment for asbestos exposure and 1.09 (95% CI 0.94–1.27) after it; the corresponding RRs were 1.33 (95% CI 0.99–1.80) and 1.27 (0.94–1.72) among woodworkers with self-reported wood dust exposure.

This study found limited evidence for a small excess of laryngeal and stomach cancers among individuals reporting exposure to wood dust. However, the excess risks were limited to non-woodworkers and did not appear to be related to length of exposure for either neoplasm.

A moderate increase of rectal cancer was found in this study, which was higher in woodworkers reporting exposure to wood dust, asbestos, or formaldehyde. However, it was based on a small number of deaths, yielding nonsignificant results, and did not show a trend with duration of exposure to wood dust. The results for colon cancer did not indicate any association with employment as a woodworker or exposure to wood dust. Excess risks for either rectal or colorectal cancer have been reported in studies of wooden pattern and model makers [Swanson and Belle, 1982; Swanson et al., 1985; Tilley et al., 1990] and occasionally in studies of other groups of woodworkers [Spiegelman and Wegman, 1985; Peters et al., 1989; Jäppinen et al., 1989]. These results were not confirmed in most of the other available studies [IARC, 1995; Demers et al., 1995], including the analysis of the previous ACS study [Stellman and Garfinkel, 1984]. Our study, therefore, adds some evidence to the conclusion that, although woodworkers may be exposed to a risk factor for rectal cancer, such an agent has not been identified and exposure to it most likely varies across wood-related industries and occupations.

We did not find any strong indication of an excess risk of other neoplasms that we considered a priori of interest, and in particular lymphatic and hematopoietic neoplasms. A weak dose–response relation was present between duration of wood dust exposure and multiple myeloma mortality, a result that was reported in a systematic analysis of risk factors of multiple myeloma in the CPS-II study [Boffetta et al., 1989]. It should be stressed that among neoplasms in this group, the evidence from previous studies is somewhat stronger for Hodgkin's lymphoma [IARC, 1995], a disease that is not easy to investigate in mortality studies such as CPS-II, given its relatively low case fatality.

In this study, there are a number of exposure-related limitations that deserve discussion. First, the available work history only included the current, last, and longest-held jobs. Second, the work history lacked details regarding the specific woodworking job held and the industry of employment. Analyses of CPS-I [Stellman and Garfinkel, 1984] found that the majority of participants who were classified as woodworkers reported employment as carpenters. In CPS-I, information on woodworking subspecialities such as carpentry was obtained via a manual search of and transcription from the original questionnaires; a comparable project has not yet been carried out for CPS-II. Employment as a carpenter might explain exposure to asbestos, which is common in the construction industry. Both these problems are likely to lead to nondifferential misclassification of exposure and therefore to false-negative results: they may be, together with small numbers, an explanation of the lack of an association with sino-nasal cancer mortality.

Third, the information regarding specific exposures was self-reported, based on a checklist. Although this represents an improvement over reporting of job title alone, the validity and reliability of data obtained with this method may be low due to selective recall or differences in each individual's criteria for what constitutes exposure, possibly leading to both differential and nondifferential misclassification. In particular, it is noteworthy that only 55% of woodworkers reported regular exposure to wood dust. A possible explanation is that woodworkers have different criteria for ''regular'' exposure than other individuals, and tend to report only high, prolonged exposure. This would have the effect of underestimating the effect of wood dust exposure among woodworkers.

Although this study was prospective in design, it had a relatively short follow-up time and used death as an endpoint, so that some of the participants of the study were likely to have been diagnosed with disease before filling out the questionnaire. Recall bias is not likely to have been an issue in regard to work history but may be of concern in regard to the self-reported ''regular'' exposures, particularly for asbestos, which is a recognized carcinogen. For example,

a person who had been diagnosed as having lung cancer may have been more likely to have reported asbestos exposure because they were aware of the association, due to being asked by a health care provider or a workers' compensation lawyer. To assess the potential impact of recall bias on the results, we repeated the analyses after excluding persons who reported they were sick at the time of interview. This eliminated a large number of cases and reduced the stability of the estimates derived from the Poisson regression models. The general effect of this exclusion was a reduction in the risk ratios association with wood dust exposure among non-woodworkers, and a reduction in precision for all estimates, but the main study findings generally held. For example, after excluding sick participants, the risk of lung cancer among persons reporting wood dust exposure alone was not elevated (RR = 1.00, 95% CI = 0.86–1.17), while the risk among those reporting both wood dust exposure and a woodworking job remained slightly elevated (RR = 1.19, 95% CI = 0.89–1.60).

In conclusion, we observed an excess of lung cancer among woodworkers which appeared to be associated not only with wood dust but also with exposure to asbestos and formaldehyde. No other convincing associations between wood dust exposure or employment in woodworking occupations and the risk of common cancers were observed. However, this study had limited power to examine associations with rare cancers and some associations may have been obscured due to misclassification of exposure. The strengths of the study were the size of the exposed cohort, the prospective design of the study, the availability of information on exposure to wood dust, asbestos, and formaldehyde, as well as smoking, and that comparisons were made with an appropriate reference group. An excess risk of non-malignant respiratory disease was also observed among persons reporting wood-related occupations in this CPS-II cohort [Demers et al., 1998].

REFERENCES

Acheson ED, Pippard EC, Winter PD (1984): Mortality of English furniture makers. Scand J Work Environ Health 10:211–217.

Andersen SK, Jensen OM, Oliva D (1982): Formaldehyde exposure and lung cancer in Danish doctors [in Danish]. Ugeskr Laeger 144:1571–1573.

Andjelkovich DA, Janszen DB, Brown MH, Richardson RB, Miller FJ (1995): Mortality of iron foundry workers. IV. Analysis of a subcohort exposed to formaldehyde. J Occup Environ Med 37:826–837.

Bertazzi PA, Pesatori AC, Guercilena S, Consonni D, Zocchetti C (1989): Cancer risk among workers producing formaldehyde-based resins: Extension of follow-up. Med Lav 80:111–122.

Blair A, Stewart PA, Hoover RN, Fraumeni JF Jr, Walrath J, O'Berg M, Gaffey W (1987): Cancers of the nasopharynx and oropharynx and formaldehyde exposure. J Natl Cancer Inst 78:191–192.

Blair A, Stewart PA, Hoover RN (1990): Mortality from lung cancer among workers employed in formaldehyde industries. Am J Ind Med 17:683–699.

Boffetta P, Stellman SD, Garfinkel L (1989): A case-control study of multiple myeloma nested in the American Cancer Society prospective study. Int J Cancer 43:554–559.

Bond GG, Flores GH, Shellenberger RJ, Cartmill JB, Fishbeck WA, Cook RR (1986): Nested case-control study of lung cancer among chemical workers. Am J Epidemiol 124:53–66.

Breslow NE, Day NE (1987): ''Statistical Methods in Cancer Research. Vol. II, The Design and Analysis of Cohort Studies.'' Lyon, France: IARC Sci. Pub. No. 82.

Burkart JA (1982): Leukemia in hospital patients with occupational exposure to the sawmill industry (Letter). West J Med 137:440–441.

Burt RD, Vaughan TL, McKnight B (1992): Descriptive epidemiology and survival analysis of nasopharyngeal carcinoma in the United States. Int J Cancer 52:549–556.

Casanova M, Morgan KT, Steinhagen WH, Everitt JI, Popp JA, Heck Hd'A (1991): Covalent binding of inhaled formaldehyde to DNA in the respiratory tract of rhesus monkeys: Pharmacokinetics, rat-to-monkey interspecies scaling, and extrapolation to man. Fundam Appl Toxicol 17:409–428.

Demers PA, Boffetta P, Kogevinas M, Blair A, Miller B, Robinson C, Roscoe R, Winter P, Colin D, Matos E, Vainio H (1995): A pooled re-analysis of cancer mortality among five cohorts of workers in wood-related industries. Scand J Work Environ Health 21:179–190.

Demers PA, Stellman SD, Colin D, Boffetta P (1998). Non-malignant respiratory disease mortality among woodworkers participating in the American Cancer Society Cancer Prevention Study-II (CPS-II). Am J Ind Med 34:238–243.

Esping B, Axelson O (1980): A pilot study on respiratory and digestive tract cancer among woodworkers. Scand J Work Environ Health 6:201–205.

Flodin U, Fredriksson M, Persson B (1987): Multiple myeloma and engine exhausts, fresh wood, and creosote: A case-referent study. Am J Ind Med. 12:519–529.

Gardner MJ, Pannett B, Winter PD, Cruddas AM (1993): A cohort study of workers exposed to formaldehyde in the British chemical industry: An update. Br J Ind Med. 50:827–834.

Gerin M, Siemiatycki J, Nadon L, Dewar R, Krewski D (1989): Cancer risks due to occupational exposure to formaldehyde: Results of a multi-site case-control study in Montreal. Int J Cancer 44:53–58.

Heck Hd'A, Chin TY, Schmitz MC (1983): Distribution of [^{14}C]formaldehyde in rats after inhalation exposure. In Gibson JE (ed): ''Formaldehyde Toxicity.'' Washington, DC: Hemisphere, pp 26–37.

IARC (1995): ''IARC Monographs on the Evaluation of the Carcinogenic Risks to Humans, Vol. 62, Wood Dust and Formaldehyde.'' Lyon, France: International Agency for Research on Cancer.

Jakab GJ, Risby TH, Hemenway DR (1992): Use of physical chemistry and in vivo exposure to investigate the toxicity of formaldehyde bound to carbonaceous particles in the murine lung. Research Report (53), October 1992, Health Effects Institute, pp 1–39.

Jäppinen P, Pukkala E, Tola S (1989): Cancer incidence of workers in a Finnish sawmill. Scand J Work Environ Health 15:18–23.

Kauppinen TP, Partanen TJ, Hernberg SG, Nickels JI, Luukkonen RA, Hakulinen TR, Pukkala EI (1993): Chemical exposures and respiratory cancer among Finnish woodworkers. Br J Ind Med 50:143–148.

Kawachi I, Pearce N, Fraser J (1989): A New Zealand cancer registry-based study of cancer in wood workers. Cancer 64:2609–2613.

Maier H, Gewelke U, Dietz A, Thamm H, Heller WD, Weidauer H (1992): Laryngeal cancer and occupation: Results of the Heidelberg laryngeal cancer study. HNO 40:44–51.

Nam JM, McLaughlin JK, Blot WJ (1992): Cigarette smoking, alcohol, and nasopharyngeal carcinoma: A case-control study among U.S. whites. J Natl Cancer Inst 84:619–622.

Olsen JH, Moller H, Moller Jensen O (1988): Risks for respiratory and gastric cancer in wood-related occupations in Denmark. J Cancer Res Clin Oncol 114:420–424.

Partanen T, Kauppinen T, Hernberg S, Nickels J, Luukkonen R, Hakulinen T, Pukkala E (1990): Formaldehyde exposure and respiratory cancer among woodworkers — An update. Scand J Work Environ Health 16:394–400.

Partanen TJ, Kauppinen TP, Luukonen RA, Hakulinen TR, Pukkala EI (1993): Malignant lymphomas and leukemias and exposures in the wood industry: An industry-based case-referent study. Int Arch Occup Environ Health 64:593–596.

Persson B, Fredriksson M, Olsen K, Boeryd B, Axelson O (1993): Some occupational exposures as risk factors for malignant lymphomas. Cancer 72:1773–1778.

Peters RK, Garabrant DH, Yu MC, Mack TM (1989): A case-control study of occupational and dietary factors in colorectal cancer in young men by subsite. Cancer Res 49:5459–5468.

Risby TH, Sehnert SS, Jakab GJ, Hemenway DR (1990): Model to estimate effective doses of adsorbed pollutants on respirable particles and their subsequent release into alveolar surfactant. I. Validation of the model for the absorption and release of formaldehyde on a respirable carbon black. Inhal Toxicol 2:223–239.

Rothenberg SJ, Nagy PA, Pickrell JA, Hobbs CH (1989): Surface area, adsorption, and desorption studies on indoor dust samples. Am Ind Hyg Assoc J 50:15–23.

Siemiatycki J, Richardson L, Gerin M, Goldberg M, Dewar R, D'esy M, Campbell S, Wacholder S (1986): Associations between several sites of cancer and nine organic dusts: Results from an hypothesis-generating case-control study in Montreal. Am J Epidemiol 123:235–249.

Spiegelman D, Wegman DH (1985): Occupation-related risks for colorectal cancer. J Natl Cancer Inst 75:813–821.

Stayner LT, Elliott L, Blade L, Keenlyside R, Halperin W (1988): A retrospective cohort mortality study of workers exposed to formaldehyde in the garment industry. Am J Ind Med 13:667–681.

Stellman SD, Garfinkel L (1984): Cancer mortality among woodworkers. Am J Ind Med 5:343–357.

Stellman SD, Garfinkel L (1986): Smoking habits and tar levels in a new American Cancer Society prospective study of 1,200,000 men and women. J Natl Cancer Inst 76:1057–1063.

Stellman SD, Boffetta P, Garfinkel L (1988): Smoking habits of 800,000 American men and women in relation to their occupations. Am J Ind Med 13:43–58.

Swanson GM, Belle SH (1982): Cancer morbidity among wood workers in the U.S. automotive industry. J Occup Med 24:315–319.

Swanson GM, Belle SH, Burrows RWJ (1985): Colon cancer incidence among modelmakers and patternmakers in the automobile manufacturing industry. A continuing dilemma. J Occup Med 27:567–569.

Tilley BC, Johnson CC, Schultz LR, Buffler PA, Joseph CLM (1990): Risk of colorectal cancer among automotive pattern and model makers. J Occup Med 32:541–546.

Vaughan TL, Davis S (1991): Wood dust exposure and squamous cell cancers of the upper respiratory tract. Am J Epidemiol 133:560–564.