

A Nested Case-Control Study of Bladder Cancer Incidence in a Steel Manufacturing Plant

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Background A surveillance study of bladder cancer incidence in northwestern Illinois detected a number of cases who had worked in a large steel manufacturing plant. To investigate these cancers further; a nested case-control study of bladder cancer was conducted at this plant.

Methods Cases from the surveillance study were matched to company personnel files. Four controls per case were selected from company files and frequency matched on age (cases and controls were all white males). Employment histories were abstracted from company records and odds ratios calculated according to job titles and departments worked. Cases and controls who held only white collar jobs were excluded from the analysis.

Results Results for 16 cases and 75 controls showed elevated odds ratios for heaters ($OR = 21.1$, 95% CI = $2.2-205.8$) based on three cases. Heaters monitored electric reheat furnaces and may have been exposed to polycyclic aromatic hydrocarbons. Previous studies have shown moderate risk for bladder cancer among furnace operators, but most of these studies were also based on a small number of cases.

Conclusions Additional studies of furnace operators' exposures and cancer risk are needed to investigate these results further. *Am. J. Ind. Med.* 34:393-398, 1998. © 1998 Wiley-Liss, Inc.

KEY WORDS: bladder neoplasms; steel manufacturing; furnace operators; polycyclic aromatic hydrocarbons

INTRODUCTION

Medical record data collected for a surveillance study of bladder cancer incidence in northwestern Illinois revealed that a number of bladder cancer cases had worked at a single large steel and wire manufacturing plant [Mallin, 1990]. Although epidemiologic studies of steelworkers have primarily detected excess lung cancer risks [Lloyd, 1971; Blot et al., 1983; Finkelstein and Wilk, 1991; Beaumont et al., 1987; Steenland and Beaumont, 1989], elevated bladder cancer risks have been found in industries that might share similar

exposures with steelworkers, including metal workers [Schiffers et al., 1987; Houten et al., 1977; Silverman et al., 1983], machinists [Anton-Culver et al., 1992; Silverman et al., 1983; Houten et al., 1977; Howe et al., 1980; Maker et al., 1987], heaters and furnace operators [Hansen, 1992; Silverman et al., 1989a; Zahm 1987; Steenland, 1987; Houten et al., 1977], welders [Howe et al., 1980], foundry workers [Egan-Baum et al., 1981; Sherson et al., 1991; Hansen, 1991; Cordier, 1993], coal carbonization and gasification workers [Doll et al., 1972; Henry et al., 1931], and aluminum smelter workers [Thériault et al., 1984; Armstrong et al., 1986]. These workers may be exposed to a variety of agents, including solvents, cutting oils, metal fumes and dusts, polycyclic aromatic hydrocarbons (PAH), combustion gases, and vapors.

The steel plant under study was founded in 1879 as a barbed wire and field fence manufacturer. Currently, the plant includes a building with three large electric furnaces for converting raw scrap to molten steel, a casting building for producing semifinished steel, a steel rod mill, two

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structural steel mills, and a wire mill that produces field fence and packaged nails. The rod and structural mills each have gas- and/or oil-fired reheat furnaces that reheat the semifinished steel before entry into the rolling mills. The electric furnaces have the capability to produce up to two millions tons of raw steel annually.

At its peak, the company employed approximately 4,000 workers but currently employs approximately 2,500 hourly workers. Employee turnover averages 5–6% per year; many workers have been employed at the plant for their entire working careers. The plant is a major employer in a small town of 15,000 people. Because of the number of different processes used, more than 1,000 different job titles have been used at this plant.

In order to further investigate the bladder cancer risks in this plant, a nested case-control study of bladder cancer was conducted, to assess whether cases had a different plant work and exposure history than other workers at the plant.

MATERIALS AND METHODS

A list of 210 male bladder cancer cases obtained in the surveillance study [Mallin, 1990] were submitted to the company for matching to their personnel files. These cases were diagnosed between 1978 and 1985 and lived in the county in which the steel plant was located or in four adjacent counties. Only cases with pathologic confirmation were included.

In order to test the accuracy of the matching procedure, 13 cases already known to have worked at the plant were included in the list of cases submitted to the company. The personnel files that were matched were computerized in 1977 and include all employees with 10 or more years of service. Cases were matched on name, birth date, and Social Security number.

Death certificates for deceased employees were also obtained for all vested employees who died between 1977 and 1989. The list of bladder cancer cases was also matched to these death certificate names to identify plant employees among the cases.

In addition to the 13 cases already known to have worked at the plant, six more cases were identified as company employees, for a total of 19 bladder cancer cases among plant employees. All these cases were employed for at least 10 years at the plant. Ten were deceased, and nine were still living at the time the study was conducted.

A systematic random sample of four controls were selected from the plant personnel files for each of the 19 cases. Controls were frequency matched on age within 1 year. Since all cases were white males, only white male controls were selected. Controls also had to be alive within 6 months of the case's diagnosis date of bladder cancer. For one case with no matches for exact age, age criteria were increased to within 2 years of age.

Work histories were obtained from paper personnel records for the 19 cases and 76 controls. Information abstracted from personnel records included job title, department and/or plant number, and starting and ending month and year for each job. Jobs lasting less than 1 month were not included in the analysis. These would include layoff periods when employees were assigned to departments needing temporary help.

Jobs were analyzed using both company job titles and Bureau of the Census occupational codes [Bureau of the Census, 1982]. Company job descriptions were requested for jobs that could not be assigned census occupational codes. Information from these job descriptions was then used to assign an occupational code.

In order to adjust for the effects of smoking, smoking history questionnaires were also mailed to each case and control, or for deceased subjects, to their next of kin. Next of kin were identified through death certificates, employee records, pension and insurance records, obituaries, and telephone directories. Two mailings were sent and, in many cases, more than one next of kin was contacted if the initial next of kin failed to return the questionnaire.

Statistical Analysis

Age-adjusted odds ratios [Mantel-Haenszel, 1959] and 95 percent test based confidence intervals [Miettinen, 1976] were calculated for job titles and departments worked in. Smoking adjusted odds ratios were also calculated.

RESULTS

Two cases and one control who held only white collar occupations were excluded from the analysis. One case and one control who had no information on job titles or departments were also excluded, resulting in 16 cases and 74 controls for analysis.

Analyses were conducted using company job titles and department names, and according to census defined occupational groups if at least three cases were employed in that occupation, department, or plant. Owing to the small number of cases, age-adjusted odds ratios were calculated for two age groups only, 65 and younger, and older than 65 years. About one-half of the cases and one-half of the controls comprised each of these two age groups.

As shown in Table I, odds ratios were significantly elevated for the company job title of heaters (odds ratios [OR] = 21.1; 95% confidence interval [95%CI] = 2.2–206.8) and the census job title of heat-treating equipment operators (OR = 29.7; 95%CI = 5.1–173.2). Confidence intervals were wide because of the small number of cases in these jobs. The three cases employed as heaters worked as heaters or chargers for their entire employment at the plant

TABLE I. Age-Adjusted^a Bladder Cancer Odds Ratios, Number of Exposed Workers, and 95% Confidence Intervals, by Plant, Company Occupational Title,^b and Census Code Occupational Title^c for Ever Versus Never Employed

Job title/ plant	Odds ratio	No. of exposed cases	95%CI
Company job title			
Heater	21.1 ^{d,e}	3	2.2–205.8
Laborer	0.9	4	0.3–2.8
Machine operator/operator learner	1.1	3	0.3–4.4
Census job title (Code)			
Heat-treating equipment operator (472)	29.7	4	5.1–173.2
Machine operators (755, 769, 777, 779)	1.1	8	0.3–3.6
Plant number			
Plant 1	0.7	10	0.2–2.0
Plant 2	0.7	6	0.2–2.2
Plant 3	1.2	3	0.3–5.1

^aAge ≤65 vs >65 years.

^bFor jobs/plants with three or more cases ever employed.

^cBureau of the Census [1982] occupational code in parentheses.

^dLogit estimate of relative risk.

^e*p* < 0.01.

for periods of 20–40 years, and the case who worked as an annealer was employed in that occupation for 35 years. One control worked as an annealer helper for 4 years; no control had worked as a heater. Thus, ORs for heaters with 20 or more years of service compared with those with less than 20 years of service would be the same as those presented.

Other jobs with three or more cases ever employed included laborers and machinists/operators. ORs for these jobs were not elevated. ORs adjusted for 10 or more, and for 20 or more years of service produced similar results. No elevated ORs were found for any departments or for any of the three separate plant buildings.

Smoking Histories

Smoking histories were obtained for 10 of the 16 cases, and 29 of the 74 controls. On the basis of these data, all 10 cases with smoking information had ever smoked 100 cigarettes or more, compared with 83% of controls (*p* > 0.10). Among smokers, information on the number of years smoked and number of cigarettes smoked per day was available for 21 controls and eight cases. Mean pack-years was slightly higher for cases than controls (17,467 vs 16,057), but the differences were not significant.

Among the census occupational group of heaters, smoking information was available for three of the four cases and the single control, and all had smoked at least 100 cigarettes. There were too few nonsmokers to adjust for

TABLE II. Bladder Cancer Odds Ratios and 95% Confidence Intervals for Heaters, Among Smokers Only,^a Adjusted for Age^b

Job We	Odds ratios	No. of exposed cases, controls	95%CI
Heater (Verbatim)	8.4 ^c	2, 0	0.77–92.2
Heat-treating equipment operator (Census code 472)	13.9	3, 1	1.3–151.4

^aEver smoked 100 or more cigarettes.

^bAge ≤65 vs >65 years.

^cLogit estimate of odds ratio.

smoking history, so ORs for employment as a heater or annealer were calculated for smokers only (10 cases, 24 controls). ORs were still elevated for heaters (verbatim) and among the census-defined group of heaters (Table II).

DISCUSSION

A limitation of this study is the relatively small number of cases. Given the large number of different jobs in this plant, the probability of cases having worked in similar jobs is small. Despite this, the number of cases who worked as heaters or annealers was significantly higher than expected.

Another limitation is that the personnel records used to identify cases only included workers with 10 or more years of service. However, given the relatively low employee turnover at this plant, it is not likely to affect the results.

The results would also be biased if any cases who had worked at the plant were not identified in the matching process. However, because the 13 cases already known to have worked at the plant were correctly matched, it is likely that the matching process used was reliable.

It was not possible to adjust completely for the effect of smoking on the results, owing to missing data for cases and controls. However, given the data available, smoking did not appear to confound the association between heater/annealer occupations and bladder cancer.

Heaters/annealers could be exposed to a number of substances, especially PAH, including benzo(a)pyrene (BaP). Electric furnaces have been used at the plant since 1936. BaP exposure in steelworks with electric furnaces have been found to be moderately elevated in Sweden (range 0.4–2.6 mg/m³ mean BaP) [Lindstedt and Sollenberg, 1982] and Japan (range 0.43–0.58 mg/m³) [Tanimura, 1968].

The three heaters spent their entire employment at the plant as heaters or chargers, and the annealer similarly spent his entire employment in this job. Heaters monitor the "reheat" furnaces that reheat the semifinished steel billets produced from the electric furnaces. This heated steel is then put through one of the rolling mills. Historically, the reheat furnaces were both gas and oil fired but are now predomi-

TABLE III. Results from Case-Control Studies Of Bladder Cancer for Occupations of Heater, Stationary Fireman, Furnace Operator, or Related Occupations

Job title	No. of cases, controls In this job	OR, 95%CI	Smoking adjusted?	Dose response tested?	Reference
Metal Heaters	5, 4	1.9 (0.4-8.7)	No	No	Silverman et al. [1989a]
Stationary fireman or furnace operator	57, 80	1.3 (0.9-1.9)	Yes	Yes; significant trend	Silverman et al. [1989a]
Forgeman, hammerman, roller finisher	11, 13	1.4 (0.6-3.4)	Yes	No	Silverman et al. [1989a]
Blacksmith	7, 6	2.4 (0.7-8.2)	Yes	No	
Heat-associated occupations in plastics and rubber industry	Not given	2.8 (0.5-15.3)	Yes	No	Zahm et al. [1987]
Furnaceman, smelterman, pourer	3, 14	0.6 (0.1-2.2)	Yes	No	Silverman et al. [1989b]
Metal molder	2, 14	0.4 (0.1-1.7)	Yes	No	Silverman et al. [1989b]
Stationary fireman or furnace operator	5, 10	1.4 (0.4-5.1)	Yes	No	Silverman et al. [1989b]
Furnace workers	18, 17	1.5 (0.8-3.2)	Yes	No	Bums and Swanson [1991]
Steel foundry workers	9, 3	2.9 (0.8-10.9)	Yes	No	Cordier et al. [1993]
Blacksmiths, stokers, workers exposed to hot metal	9, 12	2.3 (0.9-6.2)	Yes	No	Schiffman et al. [1987]
Thermal power station worker and furnaceman	13, 6	2.2 (0.8-5.6)	No	Yes, $p = 0.32$ smoking adj.	Kunze et al. [1992]
Gas worker	6, 1	6.0 (0.9-38.5)	No	No	Kunze et al. [1992]
Furnace, forge, foundry rolling mill workers	12, 17	RR <1 (CI NA)	Yes	No	Anthony and Thomas [1970]

CI, confidence interval; NA, not available.

nantly gas fired. Chargers operate machines to push billets into the reheat furnace, while annealers operate industrial heating units for annealing wire. Heaters, chargers, and annealers are all exposed to heat, gas, and hot materials.

Several case-control studies have detected elevated bladder cancer risks among workers in heat-associated occupations, including furnace operators, although most of the elevated risks were not statistically significant (Table III). One study found no elevated risk among furnacemen/smelterman/pourers [Silverman et al., 1989b], while three studies including the latter found risks ranging from 1.3 to 2.2 for stationary firemen or furnace operators [Silverman et al., 1989a,b; Kunze, 1992]. Varying definitions of furnace operators as well as differences in exposures may account for these different results.

Mortality studies of bladder cancer have also found elevated risks among furnace operators [Steenland et al., 1987], and stokers [Hansen, 1992; Henry et al., 1931] (Table IV). Most of these studies were based on a small number of furnace operators that limited the ability to detect significantly elevated risks, particularly if the risks were small.

Exposure to PAH, particularly BaP exposure has been associated with bladder cancer risks in studies of workers in aluminum reduction plants exposed to BaP [Thériault et al., 1984] and in aluminum smelters with increasing tar expo-

sure [Gibbs, 1985; Spinelli et al., 1991; Risch et al., 1988; Armstrong et al., 1986], and in case-control studies among workers determined to have frequent PAH exposure [Clavel et al., 1994; Bonassi et al., 1989]. With one exception [Gibbs, 1985], all these studies were **smoking** adjusted. A Montreal case-control study did not detect elevated bladder cancer associated with coal tar pitch or benzo(a)pyrene exposure but did find a threefold excess risk among workers with substantial exposure to natural gas combustion products [Nadon et al., 1995]. A Swedish record linkage study found slightly elevated relative risks for bladder cancer among workers exposed to combustion gases from wood or oil [Steineck et al., 1989]. A recent literature review concluded that occupational exposures to PAH increase the risk of both lung and bladder cancers [Mastrangelo et al., 1996].

Results from this study are consistent with results from other case-control studies of furnace operators and workers with PAH exposure. Since furnace operators generally make up a small proportion of workers within a plant, studies that have analyzed risks among these workers and have had limited power to detect significantly elevated risks. Documentation of PAH and other exposures among furnace workers in steel and other industries is needed to further assess any dose-related bladder cancer risks among these workers.

TABLE IV. Results from Bladder Cancer Mortality Studies for Occupations of Heater, Stationary Fireman/Furnace Operator and Related Occupations

Job title	No. of exposed cases, source of occupation	OR/SMR ^a 95% CI	Smoking adjusted?	Dose response tested?	Reference
Furnace operators	U.S. death certificates 6 exposed deaths	OR = 6.0 $p < 0.01$ CI NA	No	No	Steenland et al. [1987]
	U.S. C i Directories 13 exposed deaths	OR = 2.50 $p < 0.05$ CI NA	No	Yes $p < 0.01$ for 20+ yr employment	
Oven workers (exposed to wood soot)	Swedish census	RR = 1.1 (0.5–2.1)	No	No	Steineck et al. [1989]
Stokers in metal industry	Danish census 14 exposed deaths	SMR = 147 (80–246)	No	No	Hansen [1992]
Gas stoker	England/Wales Census 7 exposed deaths	SMR = 156	No	No	Henry et al. [1931]
Brick kiln/oven men	England/Wales Census 4 exposed deaths	SMR = 200	No	No	

CI, confidence interval; OR, odds ratio; SMR, standardized mortality ratio.

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