Exhibit 227

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Risk of urinary bladder cancer among Blacks and Whites: the role of cigarette use and occupation

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A case-control study was conducted in the United States to examine the relationship between urinary bladder cancer, usual occupation and industry, and cigarette smoking. A total of 2,160 bladder cancer cases and 3,979 colon and rectum comparison cases, with complete histories of occupation and tobacco use, were included in the analysis. Ever having smoked cigarettes significantly elevated bladder cancer risk (odds ratio = 2.4). A dose-response relationship was demonstrated between bladder cancer and pack-years of smoking, usual number of cigarettes smoked per day, and number of years having smoked. This study observes greater risk of urinary bladder cancer due to cigarette smoking among Black males and females than among White males and females. A significant excess of bladder cancer was found among armed services personnel; this excess was restricted to White males when the analysis was performed separately by race. Black males with 'mechanic' as their usual occupation had a significant sevenfold excess of bladder cancer. The population attributable risks for occupation and smoking were 25 percent and 51 percent, respectively. The results demonstrate the strength of the association between cigarette smoking and bladder cancer and the need to control for smoking in occupational analyses.

Key words: Blacks, bladder cancer, occupational risk factors, smoking, United States.

Introduction

Awareness of the association between urinary bladder cancer and occupational exposures dates back to 1895. Since that time, numerous studies have demonstrated that workers in the dyestuff, rubber, and leather industries have an increased risk of bladder cancer. Three of the chemicals used in these industries (2-naphthylamine, benzidine, and 4-aminobiphenyl) are classified as human carcinogens by the International Agency for Research on Cancer (IARC).²

Cigarette smoking also has been associated repeatedly with bladder cancer.³⁻⁹ Other risk factors that have been studied include: coffee, artificial sweeteners, phenacetin, hair dye, and water quality.¹⁰

This paper presents the results of a case-control

study of the relationship between bladder cancer, usual occupation and industry, and cigarette smoking. The purpose of the study was to identify new leads for occupations and industries associated with bladder cancer, to confirm previous studies of workplace risks of bladder cancer, to investigate occupational risk among Blacks as well as Whites, and to examine the effect of cigarette smoking on urinary bladder cancer incidence.

Materials and methods

Cases and the comparison group included in this study are part of the Occupational Cancer Incidence Surveil-

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lance Study (OCISS).11 The OCISS is a populationbased study of occupational risk factors for cancers diagnosed among residents of the metropolitan Detroit, Michigan (United States) area. Subjects for OCISS are selected through the Metropolitan Detroit Cancer Surveillance System (MDCSS). The MDCSS, a founding participant in the SEER (Surveillance, Epidemiology, and End Results) Program, has been collecting population-based cancer data for the three-county metropolitan Detroit area since 1973. OCISS cases are selected through the MDCSS rapidreporting system, which enables investigators to enroll patients into studies within two to six weeks after diagnosis. Incident cancers occurring among White and Black females and males between the ages of 40 and 84 are enrolled into the study. Cancers selected for OCISS include: lung and bronchus, colon, esophagus, urinary bladder, rectum, liver, salivary glands, stomach, eye, melanoma of the skin, and mesothelioma.

Data collection is complete for cases diagnosed with cancer of the urinary bladder and for the comparison group—persons diagnosed with cancer of the colon or rectum. There are 2,160 bladder cancer cases and 3,979 colon and rectum comparison cases included in the analyses presented in this report. Persons diagnosed with cancers of the colon or rectum constitute the most appropriate comparison group within OCISS because their cigarette-smoking patterns are similar to those of the general population.¹² Furthermore, a comparison of the occupational distribution of the control group with that of the Detroit-area general population for the 1980 census revealed patterns similar to the general population.

Subjects or their surrogates (spouse or other first-degree relative of the subject) were interviewed by telephone. With more than 20,000 interviews conducted to date, telephone interviews were the most practical method of data collection.¹³ The interview gathered information on complete lifetime occupational history, lifetime smoking history, medical history, residential history, and demographics. The response rate for cases and the comparison group was 94 percent and 95 percent, respectively.

The lifetime work history obtained includes the occupation and industry titles of all jobs ever held, a complete description of the duties performed, the dates each job began and ended, and whether the job was full- or part-time. Coding of occupations is based primarily upon information provided in the description of the duties performed, rather than on the job title. This enables the coder to utilize specific codes that are more likely to provide leads for exposures that should be investigated in future studies. Occupation and industry data obtained by the telephone interview are

coded according to the three-digit codes of the 1980 US Census Bureau classification.¹⁴ Grouped codes were created by combining appropriate three-digit codes for occupations or industries with probable similarities in work exposures. The grouped codes were created to combine jobs with similarities in exposures, decrease the number of comparisons made in the analysis, and ensure that there are adequate numbers of subjects in most groups for analysis. The grouped codes for occupations and industries are based on reviews of the literature and consultations with an industrial hygienist and an occupational physician. Usual occupation and industry are defined by summing the total number of months a person was employed in a specific industry or occupation over the entire work history and then selecting the occupation and industry for which the person had accumulated the largest number of months of exposure. The unexposed group of occupations and industries is categorized as those with the least potential for exposure to carcinogenic agents. A list of the occupations and industries defined as 'unexposed' is shown in the Appendix.

This analysis reports risk of cancer of the urinary bladder by usual occupation and industry, utilizing both grouped codes and individual 1980 US Census Bureau codes. 14 The usual occupation or industry was defined as the occupation or industry held for the longest period of time.

The case-control analysis used unconditional logistic regression to obtain maximum likelihood estimates of the odds ratio (OR) for cigarette smoking habits and for usual occupations and industries. 15,16 ORs and their respective 95 percent confidence intervals (CI) were calculated for usual occupation and industry groups that had five or more cases. The population attributable risk (PAR) was calculated for Black and White males and females for cigarette smoking, and for Black and White males for overall occupational risk. 17 Additionally, the attributable risk (AR) for cigarette smoking among smokers was calculated by race and gender.

Results

Table 1 compares bladder cancer cases with the referent group of individuals with colon or rectum cancer on selected characteristics. Cases are more likely to be White males (65.3 percent) than referents (40.6 percent). Black males and females constitute a small proportion of both the case and control groups. Urinary bladder cancer cases and the colon and rectum cancer comparison group have similar age distributions. Interview rates with the subject were similar in both groups, although a slightly higher percentage of interviews of the comparison group occurred with surro-

Table 1. Characteristics of cases and comparison group

Study group	No.	%	No.	%	No.	%	No.	%	No.	%
	Race/sex group									
	White	males	White f	emales	Black	males	Black f	emales	То	tal
Urinary bladder cases	1,410	65.3	504	23.3	161	7.5	85	3.9	2,160	100.0
Colon and rectum comparison group	1,615	40.6	1,600	40.2	382	9.6	382	9.6	3,979	100.0
No.					Age at a	liagnosis				
	40-	54	55-	69	70	- 84			То	tal
Urinary bladder cases	242	11.2	973	45.0	945	43.8			2,160	100.0
Colon and rectum comparison group	387	9.7	1,748	43.9	1,844	46.4			3,979	100.0
		-			Interview	outcome				
	Subject in	nterview	Surro	view	inter	ogate view			T	1
			(subject	too ill)	(subject o	deceased)			То	tal
Urinary bladder cases	1,620	75.0	365	16.9	175	8.1			2,160	100.0
Colon and rectum comparison group	2,880	72.4	564	14.2	535	13.4			3,979	100.0

gates due to the death of the subject. These differences between cases and the comparison group are taken into account by adjusting for age at diagnosis, cigarette smoking habits, race, and gender in the usual occupation and industry analyses.

Table 2 compares the risk of urinary bladder cancer associated with cigarette smoking among Black males, Black females, White females, and White males, separately. Black males have consistently higher levels of elevated risk, regardless of whether cigarette smoking is measured by pack-years, usual number of cigarettes per day, or number of years smoked. At 30 to 59.9 pack-years, 20 or more cigarettes smoked per day, and 40 or more years of cigarette smoking, Black males have a fourfold or greater elevated risk of bladder cancer while the risk for White males is between 2.6 and 2.9. Both Black men and White men have increasing risk of urinary bladder cancer with increased levels of cigarette smoking. Similarly, Black females have higher risk than White females of urinary bladder cancer associated with cigarette smoking. The OR for Black females at 60 or more pack-years is greater than five, compared to 3.5 for White females. Black women who smoke cigarettes for more than 40 years have an OR of 7.4 compared to 3.3 among White women.

The usual occupation and industry analysis includes groups with five or more cases and is defined for this study as having potential for exposure to carcinogens (Tables 3 and 4). Armed services personnel had a statistically significant elevated OR (3.2). A significantly decreased OR (0.5) was observed for health care professionals.

Among all cases combined (Table 4), some 'usual industry' groups had nonsignificant elevated ORs. These industry groups included: wood manufacturing (OR = 2.5); other transportation manufacturing (OR = 2.2); and drug manufacturing (OR = 1.6). A significant decrease in bladder cancer risk was found in the machinery manufacturing industry (OR = 0.7).

In the assessment of usual occupation, separately for White males and Black males (tables not shown), it is observed that the increase in bladder cancer among armed services personnel is restricted to White males (OR = 2.8). Among Black males, there was a significant excess of bladder cancer among mechanics (OR = 7.5).

The analysis of usual industry for White and Black males separately did find some industries with elevated risk; however, none of these industries were significantly elevated.

In addition to these grouped occupations and industries, we calculated ORs for all males for individual occupations and industries (based upon single Census Bureau codes) that had at least five cases for a single code category. Significantly elevated ORs were observed for two specific occupations: armed services personnel (OR = 2.8, CI = 1.2-6.8) and postal clerks (OR = 6.1, CI = 1.0-36.2). Hardware sales was the only individual industry with a significantly elevated risk among urinary bladder cancer cases (OR = 9.5,

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Table 2. Risk of bladder cancer by race, gender, and cigarette smoking habits; odds ratio (OR) estimates

Cigarette smoking habits	Cases	Controls	OR ^a	CI_P	Cases	Controls	OR^a	CI_{ρ}
		W	hite males			В	lack males	······································
Never smoked	233	499	1.0		29	145	1.0	
Ever smoked	1,176	1,112	2.3	(1.9 - 2.7)	132	237	3.0	(1.9-4.8)
Pack-years								, ,
< 30	248	348	1.5	(1.2 - 1.9)	38	106	1.9	(1.1 - 3.4)
30-59.9	456	378	2.6	(2.1 - 3.2)	48	71	4.0	(2.2 - 6.9)
60-89.9	226	181	2.7	(2.1 - 3.5)	20	22	4.7	(2.2 - 9.7)
≥ 90	194	145	3.0	(2.3 - 3.9)	12	14	4.8	(2.0-11.7)
Usual number of cigarettes per day								
1 - 19	174	225	1.7	(1.3 - 2.1)	41	95	2.3	(1.3-4.0)
20	417	383	2.4	(1.9 - 2.9)	50	81	3.6	(2.0-6.1)
> 20	552	464	2.6	(2.1 - 3.1)	34	46	4.3	(2.3-7.9)
Number of years smoked	·							
1-10	37	70	1.1	(0.7 - 1.7)	5	14	2.1	(0.7 - 6.4)
11-20	75	118	1.3	(0.9 - 1.8)	6	17	2.0	(0.7 - 5.5)
21-30	181	188	2.0	(1.5 - 2.6)	15	40	1.9	(0.9 - 4.0)
31-40	280	260	2.3	(1.8-2.9)	23	51	2.4	(1.2-4.6)
> 40	572	444	2.9	(2.3-3.5)	72	99	4.1	(2.4-6.8)
		Wł	nite female	·s		Bla	ack female	es :
Never smoked	191	944	1.0		28	235	1.0	
Ever smoked	313	656	2.4	(1.9 - 2.7)	56	146	3.8	(2.2-6.4)
Pack-years				,				,
< 30	100	298	1.7	(1.2 - 2.2)	26	77	3.1	(1.7 - 5.8)
30-59.9	134	234	2.9	(2.2-3.7)	14	41	3.8	(1.7 - 8.2)
60-89.9	42	61	3.5	(2.3-5.4)	4	8	5.0	(1.4-18.9)
≥ 90	19	34	2.7	(1.5-4.9)	2	4	5.2	(0.8-32.0)
Usual number of cigarettes per day								
1-19	97	257	1.9	(1.4-2.5)	29	73	3.7	(2.0-6.7)
20	125	243	2.6	(2.0-3.4)	11	47	2.5	(1.1 - 5.6)
> 20	81	137	3.0	(2.1-4.1)	8	21	3.7	(1.4-9.5)
Number of years smoked								
1-10	12	70	0.8	(0.4 - 1.6)	1	14	0.6	(0.1-4.5)
11-20	16	69	1.1	(0.6-2.0)	2	10	1.6	(0.3-8.1)
21-30	37	110	1.6	(0.9-2.8)	9	25	2.9	(1.1-7.5)
31-40	83	159	2.5	(1.9-3.5)	9	39	2.0	(0.8-4.8)
>40	152	230	3.3	(2.5-4.3)	32	45	7.4	(3.8-14.2)

^a Adjusted for age at diagnosis.

CI = 1.0-86.1). There were inadequate numbers of cases to evaluate Black and White males separately within single occupations or industries.

Attributable risks (AR) were calculated for cigarette smoking by race and gender. The AR estimate for smoking among White male smokers was 55.8 percent and 64.0 percent among Black male smokers. The AR estimates for smoking among females were slightly higher than for males, 57.6 percent among White female smokers compared to 68.8 percent among Black female smokers. Because previous studies have presented PARs for smoking and occupation, we calculated PARs for comparison. The overall PARs for occupation and smoking in the present study were 25 percent and 51 percent, respectively. White males had

PAR estimates of 5.9 percent for occupation and 46.6 percent for cigarette smoking. Black males had higher PAR estimates: 10.9 percent for occupation and 52.4 percent for cigarette smoking. The PAR estimates for cigarette smoking among women were somewhat lower than among men. For White women, the PAR estimate for cigarette smoking was 35.8 percent, for Black women, 45.5 percent.

Discussion

This study shows a strong association between cigarette smoking and cancer of the urinary bladder. A twofold excess of bladder cancer was found among ever-smokers. A dose-response effect was observed for

^b CI = 95% confidence interval.

Table 3. Crude and adjusted odds ratios (OR) for usual occupation among urinary bladder cancer cases

Occupation	Cases	Controls	Crude OR	Adjusted OR ^a	CI_P
Exposed occupational groups					
Police officers	22	26	2.1°	1.0	0.5 - 1.8
Construction administrators	6	2	7.6°	4.8	0.9-24.9
Chemical workers	26	42	1.6	0.7	0.4-1.2
Engineers, NEC	11	11	2.5°	1.0	0.4-2.4
Electrical workers	46	48	2.4°	1.2	0.8-1.9
Industrial engineers	29	52	1.4	0.7	0.4-1.2
Agricultural workers	23	35	1.7	1.2	0.7-2.2
Health professionals	12	45	0.7	0.5°	0.2-0.9
Driver sales	22	16	3.5°	1.7	0.9-3.4
Salesworkers—exposed	56	59	2.4°	1.1	0.7 - 1.7
Laborers	42	69	1.5°	1.0	0.6-1.5
Postal workers	10	17	1.5	1.0	0.4 - 2.4
Stock clerks	22	33	1.7	0.8	0.5 - 1.5
Assemblers	119	147	2.0°	1.1	0.9-1.5
Production inspectors	46	55	2.1	1.2	0.8-1.9
Private household workers	13	54	0.6	1.2	0.6-2.4
Firefighters	6	10	1.5	0.8	0.3 - 2.2
Food workers	20	44	1.1	1.1	0.6-1.9
Janitors and cleaners	33	61	1.4	1.0	0.6 - 1.5
Hairdressers	11	22	1.3	0.9	0.4 - 1.9
Woodworkers	30	34	2.2°	1.0	0.6-1.6
Mechanics	50	50	2.5°	1.2	0.8-1.9
Machine repairers	33	43	1.9°	1.0	0.6-1.6
Roofers	5	3	4.2	1.4	0.3 - 5.9
Molders	5	13	1.0	0.8	0.2-2.4
Tool and die workers	89	115	1.9°	0.9	0.6 - 1.2
Masons	11	16	1.7	0.8	0.3 - 1.8
Painters	30	35	2.2	1.1	0.7 - 1.9
Plumbers	25	18	3.5°	1.5	0.8-2.9
Crafts, NEC	31	47	1.7°	0.9	0.6 - 1.5
Metal finishers	74	90	2.1°	1.2	0.8 - 1.7
Furnace workers	18	17	2.7°	1.5	0.8-3.2
Dressmakers and tailors	5	9	1.4	1.4	0.4 - 4.4
Printers	12	19	1.6	0.9	0.4 - 1.9
Power plant operators	7	8	2.2	1.0	0.4-3.0
Machine operators	51	67	1.9°	1.1	0.7-1.6
Dry cleaning workers	8	14	1.4	1.9	0.7-4.9
Welders	24	47	1.3	0.7	0.4 - 1.2
Drivers	48	87	1.4	0.7	0.5 - 1.0
Railroad workers	5	8	1.6	0.7	0.2 - 2.4
Material movers	30	61	1.2	0.6	0.4 - 1.0
Armed services personnel	18	7	6.5°	3.2°	1.3 - 7.9
Computer programmers	10	21	1.2	0.6	0.2 - 1.2
Health technicians	12	34	0.9	1.5	0.7 - 3.0
Unknown	11	18	1.5	1.1	0.5-2.4
Jnexposed	812	2,048			

^a Adjusted for cigarette smoking, race, gender, and age at diagnosis.

pack-years of smoking, usual number of cigarettes per day, and numbers of years smoked. This study observes a higher relative risk of bladder cancer due to cigarette smoking among Black males and Black females than among White males and White females. To date, it has been generally estimated that about 30 percent of urinary bladder cancer is attributable to cigarette smoking.¹⁸ Our study estimates a PAR of 51 percent, suggesting that cigarette smoking may play a larger role in human bladder carcinogenesis than previously suspected. We also observed that cigarette smoking accounts for a greater percentage of bladder cancer cases among Black smokers compared with White smokers. The AR estimates for smoking were

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^h CI = 95% confidence interval for adjusted OR.

Significant at 5% confidence level.

Table 4. Crude and adjusted odds ratios (OR) for usual industry among urinary bladder cancer cases

Occupation	Cases	Controls	Crude OR	Adjusted OR ^a	CI_P
Exposed industry groups					
Farming	16	24	1.6	1.3	0.6-2.5
Mining	5	7	1.8	0.9	0.3-3.0
Construction	133	164	2.0°	0.9	0.7-1.2
Non-ferrous primary metal manufacturing	5	13	0.9	0.5	0.2 - 1.4
Ferrous primary metal manufacturing	47	41	2.8°	1.3	0.8-2.1
Clay manufacturing	5	13	0.9	0.4	0.1 - 1.2
Food manufacturing	36	38	2.3°	1.3	0.8-2.1
Beverage manufacturing	8	14	1.4	0.6	0.2 - 1.5
Textile manufacturing	6	12	1.2	0.9	0.3 - 2.6
Printing	22	41	1.3	0.7	0.4-1.2
Drug manufacturing	10	8	3.1°	1.5	0.6-4.2
Chemical manufacturing	13	20	1.6	0.6	0.3-1.2
Rubber-plastic manufacturing	20	22	2.2°	1.3	0.7-2.6
Wood manufacturing	9	6	3.7°	2.5	0.8-7.6
Fabricated metal manufacturing	32	56	1.4	0.6	0.4 - 1.0
Machinery manufacturing	86	115	1.8°	0.7°	0.5-1.0
Computer manufacturing	13	22	1.4	0.9	0.4-1.9
Appliance manufacturing	13	18	1.8	0.9	0.4-1.9
Automobile manufacturing	506	709	1.8°	0.9	0.7-1.0
Aircraft and space manufacturing	7	10	1.7	0.8	0.3-2.2
Other transportation manufacturing	7	7	2.5	2.2	0.5-2.2
Miscellaneous manufacturing	11	17	1.6	1.0	0.6-6.3
· ·	12	21	1.4	0.7	
Railroads			1.4		0.3-1.4
Bus and truck transport	36	61		0.6	0.4-1.0
Post office	19	29	1.6	1.0	0.5 - 1.9
Gas and electric utilities	28	40	1.7°	0.8	0.5 - 1.4
Automobile sales	31	29	2.6°	1.2	0.7-2.2
Lumber sales	6	8	1.8	0.8	0.3 - 2.5
Hardware sales	11	16	1.7	0.8	0.4 - 1.9
Drug sales	6	15	1.0	0.7	0.3 - 2.0
Oil and gas sales	14	11	3.1°	1.4	0.6-3.2
Liquor sales	6	6	2.5	1.2	0.4-4.3
Miscellaneous sales	22	27	2.0°	0.9	0.5 - 1.8
Building services	6	13	1.1	0.5	0.2 - 1.3
Automobile repair	12	20	1.5	0.5	0.2 - 1.1
Private households	14	66	0.5°	0.8	0.4 - 1.5
Hotels and motels	7	12	1.4	1.0	0.3-2.9
Dry cleaners and laundries	15	27	1.4	1.2	0.6-2.4
Beauty salons	10	25	1.0	0.7	0.3 - 1.5
Medical offices	10	27	0.9	0.6	0.3 - 1.3
Hospitals	20	78	0.6	0.6	0.3 - 1.1
Engineering services	10	11	2.2	1.1	0.4 - 2.7
Armed services	20	26	1.9°	0.9	0.5 - 1.6
Unknown	10	16	1.5	0.9	0.4-2.3
Unexposed	779	1,918			

^a Adjusted for cigarette smoking, race, gender, and age at diagnosis.

higher among Black male (AR = 64.0 percent) and female (AR = 68.8 percent) smokers compared to White male (AR = 55.8 percent) and female (AR = 57.6 percent) smokers. The difference in the attributable risk estimates observed between Black and White males and females may be due to a greater susceptibility of Blacks to tobacco carcinogens or to a lower rate of exposure to other risk factors among Blacks.

In a recent study, PARs for bladder cancer due to cigarette smoking were higher in White males than Black males. These investigators reported a 36 percent PAR for cigarette smoking among Black males compared with the 52.4 percent PAR observed in the present study. Unlike the study by Harris et al, the present study found significant, increasing risk of bladder cancer with increasing levels of cigarette-smoking

^b CI = 95% confidence interval for adjusted OR.

for all four race/gender groups. One difference between these two studies that may explain the variant findings is that the current study is population-based, while the previous is hospital-based. The higher cigarette-smoking risk among Black males and females is particularly important in view of the fact that the incidence of urinary bladder cancer among Black males (16.7 per 100,000) and females (5.9 per 100,000) is substantially lower than among White males (33.0 per 100,000) and females (7.3 per 100,000).²⁰

The results of the present study show an association between military service as a usual occupation and bladder cancer. When comparing results for White males and Black males separately, the increased risk was limited to White males. The usual occupation code 'armed services' was assigned regardless of the duties performed while in the service. Overall, there was no single exposure that might explain the excess of bladder cancer among armed services personnel.

An important finding of our study was the increased risk of bladder cancer in Black males with a usual occupation of automobile mechanic. Black males had a sevenfold increase in bladder cancer as compared with the comparison group. Previous studies have shown an association between bladder cancer and mechanics^{7,21-24} but none of these studies observed an increase among Black males. The results from the National Bladder Cancer Study found a tenfold excess of bladder cancer among White males ever employed as auto mechanics.²¹ However, when their data for nonWhites were analyzed separately, the OR for mechanics was a non-significant 1.4.²⁵

A previous study of bladder cancer in the Detroit metropolitan area reported an association between diesel exhaust exposure and bladder cancer.26 The study found an increased risk of bladder cancer in the trucking industry (OR = 2.2) and among dieselexposed truck drivers (OR = 11.9). In the present study, no association was seen between truck driving and cancer of the urinary bladder (OR = 0.9, CI = 0.6-1.4). Differences in the two studies may explain the discrepant results. First, there were fewer cases in the earlier study (303 cases and 296 controls) than in the present study (2,160 cases and 3,979 comparison cases). Second, the earlier study utilized population controls, while this study utilizes colon and rectum cancer comparison cases. Third, the earlier study obtained additional information to distinguish drivers of dieselfueled trucks from drivers of gasoline-fueled trucks.

It is clear from this study that we must have direct measures of cigarette smoking to understand the role of occupational carcinogens in the etiology of bladder cancer. In the present study, there were 19 occupations and 13 industries with significantly elevated ORs which did not remain significant after adjustment for cigarette smoking habits (Tables 3 and 4). The association between cigarette smoking and bladder cancer has been shown in many studies.^{3-9,19} Estimates of the ORs for smoking and bladder cancer among these studies have averaged between 2.0 and 3.0, with some estimates as high as 10.5. Cigarette smoke contains the bladder carcinogen 2-naphthylamine, but in low concentrations.²⁷ Nitrosamines are also present in cigarette smoke and may be involved in bladder carcinogenesis.²⁷

It has been estimated previously that smoking accounts for about 30 percent of urinary bladder cancer. The PAR estimates for occupation range from 18 percent to 35 percent among men. Occupation accounts for little of the bladder cancer among females, with PAR estimates of one to six percent. Our attributable risk estimates for this population indicate that a larger proportion of cancers of the urinary bladder are due to cigarette smoking, while the proportion due to occupation falls within the range of previous estimates.

The strengths of this study are considerable. The information about cancer diagnoses used in the study were obtained from hospital medical records through routine data collection in a population-based cancer surveillance system. Over 98 percent of diagnosed cancers of the urinary bladder, colon, and rectum were confirmed microscopically.

Another strength of the study is the complete work history and cigarette smoking history obtained from each study subject or surrogate. The occupational history allowed us to determine the usual occupation and industry of subjects. As demonstrated by this study's results, an accurate assessment of occupational risk could not have been obtained without information on cigarette smoking. For 'usual occupation,' 20 categories had significantly elevated ORs before adjusting for cigarette smoking. Only one remained significant in the adjusted ORs. Thirteen 'usual industry' categories were significant before adjusting for cigarette smoking—none remained significant after adjustment.

Few investigations of occupational cancer etiology include Blacks. This study has identified elevated risks of cancer of the urinary bladder among Black males that have not been observed previously. It also demonstrates that bladder cancer risks associated with cigarette smoking and with the workplace differ between Blacks and Whites.

This study has some limitations, one of which is the large number of comparisons performed in the analysis. The number of comparisons was reduced to a certain extent by restricting the analysis to occupation and industry groups with at least five cases. Another

limitation is the lack of specific job-exposure data. Exposure data would increase our ability to identify more precisely the chemicals or other substances associated with the observed increases in bladder cancer. However, it was necessary to limit the length of the interview to support the collection of data on the large number of subjects included in this study. This type of study is useful to select occupations and industries at high risk of urinary bladder cancer within which more specific investigations of exposures can be conducted. Classifying occupation and industry groups as 'exposed' or 'unexposed' based on the literature, as we did, may result in a certain amount of misclassification. However, since exposure classification of occupation and industry groups was made prior to analysis and independent of case or comparison status, any misclassification will be nondifferential. If bias does exist in our risk estimates, they will be biased toward the null, and therefore underestimate occupational risk.

The results of this study provide some important leads in the etiology of cancer of the urinary bladder. Military service was associated consistently with bladder cancer, especially among White males. Such an association has not been reported previously and should be explored further to determine specific exposures and military assignments associated with this elevated risk. Another new observation was the excess of bladder cancer among Black males whose usual occupation was automobile mechanic. Further investigation of this result should determine whether Black male mechanics are more likely than White males, for example, to work in small repair shops or gas stations that are exempt from OSHA exposure regulations. This finding emphasizes the importance of investigating racial diversity in occupational bladder cancer etiology. This study indicates that cigarette smoking may play a more important role in human bladder carcinogenesis than previously suspected. It is clear that future studies of occupational bladder cancer risk must thoroughly assess cigarette smoking history in order to adequately evaluate the role of workplace exposures.

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Appendix

Nonexposed occupation and industry groups						
Occupation groups	Industry groups					
Administrators	Communications					
Financiers	Paper sales					
Buyers/advertisers	Clothing sales					
Health administrators	Food stores					
Real estate sales	Department stores					
Statisticians	Appliance/furniture sales					
Teachers	Restaurants					
Social workers/clergy	Banks					
Social scientists	Real estate					
Bookkeepers	Advertising					
Artists	Business services					
Lawyers	Personal services					
Library/museum workers	Entertainment services					
Writers	Legal services					
Radio/TV announcers	Schools					
Sales workers	Child care					
Clerical workers	Social services					
Communication equipment operators	Art					
Food workers	Religion					
Housewives	Government					
Students	Justice					
Unemployed	Volunteer services					

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