Motor Exhaust-related Occupations and Bladder Cancer

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ABSTRACT

The relationship between employment in occupations with potential exposure to motor exhaust and bladder cancer risk was examined based on interviews conducted with 1909 white male bladder cancer patients and 3569 population controls during the National Bladder Cancer Study, a population-based, case-control study conducted in ten areas of the United States. Our findings indicated that males usually employed as truck drivers or deliverymen have a statistically significant, 50% increase in risk of bladder cancer. Overall, a statistically significant trend in risk with increasing duration of truck driving was observed. This trend was particularly consistent for drivers first employed at least 50 years prior to diagnosis. Of these, truck drivers employed 25 years or more experienced a 120% increase in risk. Elevations in risk were also suggested for taxicab and bus drivers. These findings, coupled with experimental evidence of the mutagenicity and possible carcinogenicity of motor exhaust emission particulates, suggest a role for motor exhaust exposure in human bladder carcinogenesis.

INTRODUCTION

This study examines the relation between the risk of developing cancer of the urinary bladder and employment in occupations with potential exposure to motor exhaust (motor exhaust-related occupations). A recent analysis of data from one of the ten centers in the National Bladder Cancer Study suggested that truck drivers and perhaps others occupationally exposed to motor exhaust have an increased risk of bladder cancer (1). In the current study, data from all ten areas were pooled to further evaluate this suggested association. The large numbers of subjects employed in motor exhaust-related occupations in the national study afforded the opportunity to estimate risks in detail with more precision than is typical in case-control studies.

Previous epidemiological studies concerning motor exhaust exposure have focused primarily on lung cancer and diesel exposure. Of these, few studies have demonstrated a positive association (2). Experimental data, however, have suggested that certain constituents of diesel exhaust are mutagenic and carcinogenic (3). Awareness of the importance of the potential carcinogenicity of diesel exhaust has recently been reflected in the United States Environmental Protection Agency's promulgation of the first Unites States standard for particulate emissions from heavy-duty diesel engines (4). Although more rigid standards for both light-duty and heavy-duty diesel vehicles are scheduled to go into effect soon, the adverse health effects associated with diesel exhaust exposure are not well understood.

The current study suggests that examination of sites other than the point of direct exposure may be critical to understanding the potential carcinogenic effects of diesel and gasoline engine exhaust.

MATERIALS AND METHODS

For the purpose of this occupational analysis, the study group was restricted to 1909 white male cases and 3569 white male controls. The case series consisted of all histologically confirmed cases of carcinoma of the urinary bladder first diagnosed during a 1-year period that began in late 1977 or early 1978. Cases were identified through population-based cancer registries in areas of the United States that participate in the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) Program (i.e., New Jersey, Atlanta, Detroit, New Orleans, San Francisco, Seattle, Connecticut, Iowa, New Mexico, and Utah). Only cases that occurred among residents of the study areas who were between the ages of 21 and 84 years were considered eligible for study.

The control series was drawn from the general population of the study areas. Cases and controls were frequency matched for age (within 5 years) and geographic area. Approximately two controls were selected for each case. We chose controls ages 21–64 years using a method of random digit dialing (5). Controls ages 65–84 years consisted of a stratified random sample drawn from the Health Care Financing Administration’s lists of the population over age 64 years for each study area.

Interviews were usually conducted in the subjects’ homes by a trained interviewer. Of the males identified for study, we interviewed 75% of the cases, 84% of the controls ages 21–64 years, and 83% of the controls ages 65–84 years. For more detailed information regarding response rates, see Hartge et al. (6).

The questionnaire was designed to elicit detailed information on every job a subject had held for at least 6 months since the age of 12 years. We also obtained information on smoking history, coffee consumption, artificial sweetener use, residential history, source of drinking water, fluid intake, use of hair dyes, and medical history.

The association between employment in a motor exhaust-related occupation and bladder cancer risk was measured by the relative risk estimated by the odds ratio. In all relative risk computations, the unexposed group included only subjects who were never employed in a motor exhaust-related occupation. Adjusted relative risks were estimated by the maximum likelihood method (7). The data were initially stratified by age, smoking, coffee drinking, employment in other motor exhaust-related occupations, occupational exposure to other high-risk substances, history of urinary tract infections, urbanization, and geographic area. Age (in four categories: 21–44 years, 45–64 years, 65–74 years, and 75–84 years) and smoking (in five categories: nonsmoker, less than 1 pack per day, 1 to less than 2 packs per day, 2 to less than 3 packs per day, and 3 or more packs per day) were the only factors for which adjustment had an impact on the estimates of relative risk; thus, only age- and smoking-adjusted relative risks were included in this presentation unless otherwise specified. Two-sided 95% confidence intervals for the adjusted relative risk estimates were computed by Gart's interval estimation procedure (7). Two-tailed significance tests for trend were computed by the Mantel-Haenszel procedure (8).

All analyses were initially done excluding observations from Detroit since the data from that center generated the hypothesis under investigation in the present study. When we repeated the analyses based on the total study group, estimates of relative risk were almost identical to our initial estimates. For this reason and because of the added precision gained by greater numbers, only relative risk estimates based on the total study group were given.

RESULTS

Table 1 shows the relative risks estimated for males ever or usually employed as a truck driver or deliveryman (subsequently
MOTOR EXHAUST AND BLADDER CANCER

Table 1 Numbers of cases and controls "ever" and "usually" employed in each motor exhaust-related occupation category, and relative risks

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Cases</th>
<th>Controls</th>
<th>Relative Risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never any motor exhaust-related occupation</td>
<td>1353</td>
<td>2724</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Truck driver or deliveryman</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>488</td>
<td>742</td>
<td>1.3</td>
<td>1.1–1.4</td>
</tr>
<tr>
<td>Usual</td>
<td>99</td>
<td>123</td>
<td>1.5</td>
<td>1.1–2.0</td>
</tr>
<tr>
<td>Taxicab driver or chauffeur</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>77</td>
<td>92</td>
<td>1.6</td>
<td>1.2–2.2</td>
</tr>
<tr>
<td>Usual</td>
<td>10</td>
<td>3</td>
<td>6.3</td>
<td>1.6–29.3</td>
</tr>
<tr>
<td>Bus driver</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>49</td>
<td>75</td>
<td>1.3</td>
<td>0.9–1.9</td>
</tr>
<tr>
<td>Usual</td>
<td>9</td>
<td>13</td>
<td>1.5</td>
<td>0.6–3.9</td>
</tr>
</tbody>
</table>

* Eighteen males with unknown smoking history were excluded (17 were never employed in a motor exhaust-related occupation and 1 was employed as a truck driver or deliveryman).

* Relative to a risk of 1.0 for males never employed in a motor exhaust-related occupation; adjusted for age and smoking.

* Males employed in more than one motor exhaust-related occupation are included in each occupation category they were ever employed in. They are counted only once, however, in the category that represents their usual occupation.

Table 2 Numbers of cases and controls and relative risk according to duration of employment in each motor exhaust-related occupation category

<table>
<thead>
<tr>
<th>Duration of employment (yr)</th>
<th>Cases</th>
<th>Controls</th>
<th>Relative Risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never any motor exhaust-related occupation</td>
<td>1353</td>
<td>2724</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Ever truck driver or deliveryman</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>208</td>
<td>379</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>5–9</td>
<td>102</td>
<td>148</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>10–14</td>
<td>58</td>
<td>65</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td>15–24</td>
<td>59</td>
<td>52</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>25+</td>
<td>54</td>
<td>88</td>
<td>1.1</td>
<td></td>
</tr>
</tbody>
</table>

(\(x^2 = 3.89; P < 0.001\))

| Ever taxicab driver or chauffeur |       |          |               |           |
| <5                             | 44    | 48       | 1.9           |           |
| 5–9                            | 14    | 26       | 1.0           |           |
| 10+                           | 16    | 15       | 2.0           |           |

(\(x^2 = 2.47; P = 0.014\))

| Ever bus driver               |       |          |               |           |
| <5                            | 21    | 32       | 1.3           |           |
| 5–9                           | 11    | 17       | 1.2           |           |
| 10+                           | 16    | 25       | 1.3           |           |

(\(x^2 = 1.24; P = 0.20\))

* Males with unknown smoking history and/or duration of employment were excluded.

* Relative to a risk of 1.0 for males never employed in a motor exhaust-related occupation; adjusted for age and smoking.

referred to as truck drivers), taxicab driver or chauffeur (subsequently referred to as taxicab drivers), and bus driver. Statistically significant elevations in risk were seen for workers ever employed as a truck driver (relative risk, 1.3) and as a taxicab driver (relative risk, 1.6), as well as for those whose usual occupation was either truck driver (relative, 1.5) or taxicab driver (relative risk, 6.3). Statistically nonsignificant increased risks were also apparent for bus drivers. For each of these three occupational categories, relative risks for workers usually employed were higher than relative risks for workers ever employed.

Truck drivers also experienced a statistically significant increased risk with increasing duration of employment (Table 2). The relative risk for truck drivers peaked at 2.2 (confidence interval, 1.4–3.2) for those employed 15–24 years but was 1.1 for those employed 25 years or more. A consistent gradient of risk with increasing duration of employment was not observed for either taxicab drivers or bus drivers. Therefore, the remainder of the analysis focused on truck drivers.

We examined the relationship between bladder cancer risk and latent period (i.e., the interval from first employment as a truck driver to diagnosis of bladder cancer). The age- and smoking-adjusted relative risks for truck drivers by latent period were less than 30 years, 1.1; 30–39 years, 1.1; 40–49 years, 1.3; 50 years or more, 1.4. Thus, truck drivers first exposed less than 40 years prior to diagnosis experienced virtually no excess risk. Since increased risk was restricted to truck drivers with long latent periods, we reexamined risk by duration of employment among truck drivers with a latent period of 50 years or more (Table 3). A statistically significant trend in risk with increasing duration of employment was observed; the relative risk for truck drivers employed 25 years or more with a latent period of at least 50 years was 2.2 (confidence interval, 1.1–4.2). Thus, the absence of risk noted for truck drivers employed 25 years or more (Table 2) was explained by the absence of risk experienced by long-duration truck drivers with a latent period of less than 40 years.

When relative risks for truck drivers by geographic area were examined, elevations in risk were seen for truck drivers in the five areas specified in Table 4. A consistent trend in risk with increasing duration of employment was apparent for truck drivers in four of the five areas: Connecticut, New Jersey, Detroit, and Iowa. These trends were statistically significant in New Jersey (\(P = 0.014\)) and Detroit (\(P = 0.006\)) and approached significance in Connecticut (\(P = 0.058\)) and Iowa (\(P = 0.068\)). Subjects from the other study areas were combined because relative risks for the smaller areas tended to be unstable due to small numbers. Although no excess risk was observed for truck drivers in the other areas combined, long-term truck drivers in Atlanta did experience an increased risk.

We also examined the joint effect of cigarette smoking and employment as a truck driver. The age-adjusted relative risks for truck drivers by usual amount smoked were: nonsmoker, 1.3; males who smoked less than 1 pack per day, 2.0; males who smoked 1 to less than 2 packs per day, 3.0; males who smoked 2 or more packs per day, 3.6. Within each smoking stratum, the risk for truck drivers was greater than that for males never employed in a motor exhaust-related occupation, but no evidence of interaction between smoking and employment as a truck driver was apparent. When the joint effect of smoking and long-duration employment as a truck driver was considered, similar patterns were observed. No evidence of synergism between truck driving and other bladder cancer risk factors was apparent either.

DISCUSSION

The results from the entire National Bladder Cancer Study confirm the increased risk for truck drivers initially suggested for either taxicab drivers or bus drivers.
by data from one center (1). Our findings indicate that males usually employed as truck drivers have a statistically significant, 50% increase in risk of bladder cancer. Overall, a statistically significant trend in risk with increasing duration of truck driving was observed. This trend was particularly consistent for truck drivers first employed at least 50 years prior to diagnosis. Among those with such long latent periods, truck drivers employed 25 years or more experienced a 120% increase in risk. Elevations in risk were also seen for taxicab drivers and bus drivers. However, a consistent gradient in risk with increasing duration of employment was not apparent for either of these occupations. Thus, evidence of increased risk for taxicab drivers and bus drivers was not as strong as it was for truck drivers. This may reflect differences among these occupations in intensity of exposure to motor exhaust, if motor exhaust exposure is, in fact, responsible for the excess risk observed for these occupational groups.

Although not generally recognized, published results from several large surveys of occupation and mortality also lend credibility to the suggestion of an increased bladder cancer risk among workers in motor exhaust-related occupations. Our review indicated that elevations in risk were apparent for truck drivers (9–12) and for taxicab drivers (9, 10). Decoufle et al. (10) found a 50% increased risk among males employed for at least 5 years in the combined category of bus, taxicab, and truck driver. Elevated bladder cancer mortality among vehicle drivers also has been cited in the Registrar General's decennial occupational mortality analyses for England and Wales (13). In addition, exposures to motor exhaust (14), diesel and traffic fumes (15, 16), and combustion products have been associated with increased bladder cancer risk (17).

Results of this epidemiological study are also noteworthy in light of experimental evidence of the mutagenicity and possible carcinogenicity of motor exhaust emission particles. Motor exhaust emissions contain PAHs and nitro-PAHs (18, 19). In particular, the mutagenic activity of extracts from diesel particulates is much greater than that of particulates collected from gasoline engines (20, 21). Nitro-PAHs, especially nitropyrenes, appear to be involved in a substantial portion of the mutagenicity associated with diesel emissions (3, 22). In addition to being potent, direct-acting, frameshift mutagens for Salmonella typhimurium, nitropyrenes have been shown to induce mutations in cultured mammalian cells, sister chromatid exchanges, and unscheduled DNA synthesis in eukaryotes (19, 22).

Recent studies on the deposition and biological fate of nitropyrenes have shown that, in rats exposed to 1-NP-1-NP is the nitroarene that is usually in greatest abundance in environmental samples (23)] by either nose-only inhalation or injection, metabolites of 1-NP were excreted in the urine and some of these metabolites were, in fact, mutagenic (24, 25).

Two lines of evidence suggest that nitro-PAHs may be responsible for the induction of human bladder cancer. Nitro-PAHs can be metabolized to aromatic amine derivatives; certain of these agents are known to be capable of inducing urinary bladder cancer in humans (26). Furthermore, 1-NP has been reported to be carcinogenic for the rat mammary gland (27); the structurally related 4-aminobiphenyl, which induces bladder cancer in humans, also induces mammary gland tumors in the rat (27). Although the applicability of these experimental results to humans is unknown, the laboratory evidence, taken together with the epidemiological data, suggests a role for motor exhaust exposure in human bladder carcinogenesis.

Few data exist regarding the concentrations of motor exhaust to which truck drivers are exposed from either direct leakage of exhaust into the truck cab or from on-the-road exposure to traffic exhaust. Results of one study in heavy-duty diesel tractor trucks indicated statistically significant elevations in in-cab concentrations of nitrogen dioxide; limited sampling measurements showed that total hydrocarbons were also elevated (28). Additional monitoring and study of biological markers are needed, however, to characterize exposure to nitro-PAHs and PAHs among diesel- and non-diesel-exposed truck drivers.

Although the observed excess risk among truck drivers may be due to motor exhaust exposure, another possible explanation is urinary stasis. Urinary stasis has not been investigated as a risk factor for bladder cancer. However, a number of conditions that can cause urinary stasis, such as urinary obstruction and benign prostatic hypertrophy, have been associated with increased bladder cancer risk in previous studies (29, 31). If carcinogens are present in the urine, prolonged retention could increase their contact time with the bladder mucosa and thus increase the potential for development of bladder cancer. It is therefore possible that the increased risk observed among truck drivers may be partly attributable to prolonged retention of urine. Moreover, if motor exhaust does contain carcinogens or procarcinogens that are excreted in the urine, urinary stasis coupled with motor exhaust exposure may be largely responsible for the excess bladder cancer risk experienced by truck drivers.

The public health implications of these results merit consideration. Although the magnitude of risk associated with employment as a truck driver appears to be small, the number of individuals employed as truck drivers in the United States is large, approximately 2.4 million in 1980 (32). If the association between employment as a truck driver and bladder cancer is

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**Table 4 Numbers of cases and controls and relative risk according to duration of employment as a truck driver or deliveryman and geographic area**

<table>
<thead>
<tr>
<th>Area</th>
<th>&lt;10 years duration</th>
<th>10+ years duration</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Controls</td>
<td>Relative risk</td>
</tr>
<tr>
<td>Connecticut</td>
<td>39</td>
<td>73</td>
<td>1.3</td>
</tr>
<tr>
<td>New Jersey</td>
<td>82</td>
<td>160</td>
<td>0.9</td>
</tr>
<tr>
<td>Detroit</td>
<td>43</td>
<td>30</td>
<td>1.6</td>
</tr>
<tr>
<td>Iowa</td>
<td>42</td>
<td>74</td>
<td>1.2</td>
</tr>
<tr>
<td>San Francisco</td>
<td>45</td>
<td>65</td>
<td>1.6</td>
</tr>
<tr>
<td>Other</td>
<td>59</td>
<td>125</td>
<td>0.9</td>
</tr>
</tbody>
</table>

* a Relative to a risk of 1.0 for males never employed in a motor exhaust-related occupation in the specified area, adjusted for age and smoking.

* Numbers of cases and controls and relative risks for Detroit truck drivers differ from those in a previous report (1) because the occupation category "truck driver's did not include deliverymen in the previous study, whereas it does in the current study.

* Relative risks for truck drivers employed at least 10 years were: Seattle, 0.9; New Mexico, 1.2; Atlanta, 3.0; Utah, 0.8. In New Orleans, there were too few truck drivers to compute relative risks by duration (9 cases, 9 controls).

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* The abbreviations used are: PAH, polycyclic aromatic hydrocarbons; nitro-PAH, nitro-polycyclic aromatic hydrocarbons; 1-NP, 1-nitropyrene.
causal and if the proportion of males ever employed as a truck driver in our population control group reflects that in the general population of the United States, then we estimate that approximately 4%, or 1100 cases, of bladder cancer diagnosed among United States males in 1985 may be attributable to exposures incurred during employment as a truck driver. Moreover, this estimate would be substantially larger if it were expanded to include employment in all motor exhaust-related occupations.

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REFERENCES

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