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# OCCUPATION AND CANCER OF THE LOWER URINARY TRACT

PHILIP COLE, MD,* ROBERT HOOVER, MD,† AND GILBERT H. FRIEDELL, MD‡

**Lifetime occupation histories were elicited from 461 persons with transitional or squamous-cell carcinoma of the lower urinary tract, 94% of whom had a bladder tumor. This was a sample of all such persons newly diagnosed in a designated area in eastern Massachusetts during a recent 18-month period. A sample of 485 persons from the population of the entire study area provided comparable histories and serves as a control group. Occupations were classified according to two schemes developed for this study. Among men, excess risk of lower urinary tract cancer was found in 5 of 8 occupation categories where this was suspected *a priori:* dyestuffs, rubber, leather and leather products, and paint and organic chemicals. Although suspected, excess risk was not confirmed for 3 categories: printing, petroleum, and chemicals other than organic. The relative risks for men ever employed in the rubber industry (1.63) and in the leather industry (2.25) are statistically significant, $p < 0.05$. In absolute terms, the 5 risk categories account annually for 7.3 cases of lower urinary tract cancer per 100,000 men aged 20–89; this is about 18% of male bladder cancer. Among women, the comparable figures are 0.8 cases and 6% of the disease. None of the associations of bladder cancer with occupation results from any indirect association with cigarette smoking. Although requiring cautious interpretation, the data suggest increased risk in 2 occupation groups not previously suspected: cooks and kitchen workers and clerical workers.**

MORE THAN 70 YEARS AGO, REHN SUGGESTED that dyestuffs workers were at increased risk of developing a bladder tumor.[21] This has been confirmed repeatedly, and it is now recognized that risk of bladder cancer in this industry is associated with the naphthylamines,[22] not with aniline as was long suspected. Rubber[7] and cable[10] workers have also been at increased risk and the same may be true for other occupation groups.[15,22,27] Despite the significance of occupational exposures in this disease, there is little information on the occupational hazards to which a population may be subjected or on the amount of bladder cancer that may be attributable to these causes. The present study was designed to estimate the risks of bladder cancer associated with known occupational exposures and to seek previously unrecognized hazards.

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* Assistant Professor and † Teaching Fellow, Department of Epidemiology and Kresge Center for Environmental Health, Harvard University School of Public Health.

‡ Chief of Pathology, Saint Vincent Hospital; Clinical Professor of Pathology, University of Massachusetts Medical School, Worcester, Mass.

Address for reprints: P. Cole, MD, Department of Epidemiology, Harvard School of Public Health, 665 Huntington Ave., Boston, Mass. 02115.

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## METHODS

*Subjects:* This report is based on case and control groups described previously.[9] During an 18-month period, in an area in eastern Massachusetts including Boston, an attempt was made to identify all residents, aged 20 to 89, newly diagnosed with histologically confirmed transitional or squamous-cell malignancy of the renal pelvis, ureter, bladder, or urethra. Six hundred and sixty-eight cases (491 men, 177 women) were ascertained. Since 94% of the cases had a bladder tumor, the term

"bladder cancer" will be used for brevity to refer to malignancies throughout the lower urinary tract. A random sample of 510 of the cases was selected for interview. Of these, 488 were located and 470 (92%) were interviewed; usable occupation histories were obtained for 461 (356 men, 105 women). For each case, a person of the same sex and year of birth was selected at random from an age- and sex-stratified sample of the adult population of the entire study area. The sample was compiled from inclusive Residents Lists, updated annually by each of the study area towns. A random sample of 552 controls was selected from the 668 persons designated as potential controls. Of these, 534 were located and 500 (91%) were interviewed; usable occupation histories were obtained for 485 (374 men, 111 women).

*Occupation history:* The "working life" was defined as beginning at age 12 or upon leaving secondary school, if later. The period terminated at diagnosis for cases and, for controls, at the age at which the corresponding case had been diagnosed. A usable occupation history was defined as one in which at least one third of the working life was accounted for. As shown in Table 1, the histories are nearly complete for subjects meeting the requirement. For each position held for at least 6 months, and proceeding back from the most recent employment to the first, inquiry was made as to name, location and nature of the employing organization, title of position, age at starting and years spent, specific duties performed, exposure to chemicals, solutions, dusts, gases, fumes, ionizing radiation, and temperature extremes, and need for protective devices or clothing.

Higher education, military service, and housekeeping were included as "positions." Two or more positions with similar duties were combined as one "occupation." A maximum of 9 occupations was coded per subject. Only 3 male cases had engaged in more than 9 occupations. For each, the 9 occupations with the longest durations were retained. Occupations were classified according to each of two different systems by two of us who were unaware of whether information related to a case or a control.

*Classification of occupation exposures:* This classification groups together occupations with similar exposures, irrespective of the associated education, training, skills, or salary. Based on a literature review, 13 occupation categories were created and ranked from presumed highest risk of bladder cancer (01–dyestuffs manufacture and use) to lowest (13–office work) with addenda for retirement, unemployment, and unclassifiable activities. The 13 categories are listed in Table 2. For brevity, as well as reflecting our opinion prior to this study, categories 01–08 are referred to as "suspect" and categories 09–13 as "nonsuspect." Each occupation category was divided into subcategories, also ranked according to presumed decreasing risk.

TABLE 1. Mean Values for Several Measures of Occupation Experience and of Comparability of Interview Data for Cases and Controls, by Sex

| | Men | | Women | |
|---|---|---|---|---|
| | Cases | Controls | Cases | Controls |
| Age experience began | 15.8 | 15.9 | 16.7 | 16.1 |
| Years of experience | 50.5 | 49.8 | 49.4 | 49.7 |
| Per cent accounted for | 95 | 96 | 95 | 96 |
| No. of positions | 4.8 | 4.7 | 4.0 | 3.5 |
| No. of occupations | 3.5 | 3.3 | 2.6 | 2.7 |
| No. of subjects | 356 | 374 | 105 | 111 |

Occupations were assigned to subcategories on the basis of specific duties and materials used. An occupation classifiable in more than one subcategory was assigned to that with the lowest number. Originally, there were 70 subcategories, but on the basis of the distribution of occupations among cases and controls combined, this was reduced to 31. Subcategories where, due to small numbers, no meaningful comparisons could be made were merged with the most similar subcategory retained.

*Classification of occupation titles:* This classification system was to provide a large number of unique designations so that previously unrecognized hazardous occupations might emerge. The system also provided a preexisting classification scheme to assess the validity of the exposure code. The title code was modified from that used by the United States Bureau of the Census.[24] The Bureau's code (alphabetic, within social class) was consolidated and rearranged to bring together titles denoting similar exposures. However, the more common occupations were uniquely identified by this code. Occupations were assigned a title designation on the basis of title alone, without consideration of type of exposure. Originally, this modified code consisted of 177 titles and addenda. In the same way that the exposure code was reduced, it was shortened to 42 titles.

*Analytic methods:* A major difficulty in comparing the occupational experiences of

TABLE 2. Observed and Expected Numbers of Occupations among Male Cases and Estimates of Relative Risk and the Associated Confidence Limits, by Occupation Category

| Occupation category | Male case occupations | | | Rel. risk† | 95% C. L.‡ |
|---|---|---|---|---|---|
| | Obs. | Exp.* | Exp.** | | |
| Suspect | | | | | |
| 01. Dyestuffs | 7 | 3.9 | 3.2 | 2.24 | 0.67–7.56 |
| 02. Rubber, rubber products | 51 | 36.8 | 34.6 | 1.57 | 1.04–2.36 |
| 03. Leather, leather products | 79 | 41.5 | 42.4 | 2.00 | 1.37–2.90 |
| 04. Printing | 15 | 16.1 | 18.0 | 1.09 | 0.60–1.96 |
| 05. Paint | 28 | 22.7 | 26.0 | 1.17 | 0.71–1.93 |
| 06. Petroleum products | 102 | 102.4 | 108.3 | 1.00 | 0.75–1.34 |
| 07. Other organic chemicals | 14 | 10.9 | 9.2 | 1.44 | 0.76–2.73 |
| 08. Other chemicals | 18 | 20.9 | 20.4 | 0.96 | 0.54–1.71 |
| Nonsuspect | | | | | |
| 09. Fumes, dust, dirt, smoke | 71 | 91.1 | 98.1 | | |
| 10. Manufacturing (N.E.C.)*† | 109 | 116.3 | 123.4 | | |
| 11. Ranching, farming | 41 | 60.2 | 55.8 | 1.00 | — |
| 12. Service | 537 | 551.9 | 546.3 | | |
| 13. Office | 169 | 166.3 | 155.3 | | |
| Total occupations | 1241 | 1241.0 | 1241.0 | | |

* Controlled for age.
** Controlled for age and cigarette smoking.
† Relative to a risk of 1.00 for all occupations in categories 09–13, combined; controlled for age and cigarette smoking.
‡ 95% confidence limits of the relative risk.
*† Not elsewhere classified.

groups is determining a suitable unit of comparison. Cases could be compared with controls on the basis of numbers of men in each of the 13 occupation categories. This would require a decision as to whether a man should be classified on the basis of his "usual" occupation or his "most recent" occupation or whether he has "ever" been employed in each of the categories. Alternatively, cases could be compared with controls on some basis not involving numbers of men. For example, comparisons could be based on the total number of case and control occupations in each of the 13 categories or even total years accumulated in each category.

We have used "occupations" as the primary comparison unit. This has the advantage of using all the data gathered, unlike any comparison based on numbers of individuals. Moreover, with the present classification system which merged similar positions into one occupation, each occupation may be considered as an event essentially independent of other occupations held by the same individual. This, of course, would not be true of total years of experience in each category. Further, only 2.8% of male cases and 2.1% of male controls held occupations classified in more than one exposure category found in this study to be associated with increased bladder cancer risk. Nonetheless, relative risk estimates and evaluation of statistical significance, when based on numbers of occupations, probably should be considered only nominal. Because of this, two sets of results are presented using the individual as the unit of comparison,—one based on the usual occupation and one based on whether a man was ever employed in each of the suspect categories. Again, risk estimates based on the latter measure should be considered nominal since one man could count in several suspect categories. However, neither the risk estimates based on usual occupations nor the associated confidence limits need be considered nominal. Actually, risk estimates for any one suspect category are quite similar, irrespective of the unit of comparison. However, the "statistical significance" of the associations does vary.

A lesser problem concerns the reference group to be used in estimating risks. In general, when using the exposure code, risk in each suspect category is related to that in all nonsuspect categories, since these were designated *a priori*. When using the title code, which designated suspect groups *a posteriori*,

risk in each such group is related to that for all occupations.

Data from this study reveal an association of bladder cancer risk with cigarette smoking.[9] It was necessary, therefore, to determine whether any observed association of risk with occupation was indirect and due to an association of occupation with cigarette smoking. When so specified, the risk estimates were controlled for cigarette smoking using 3 categories of maximum daily cigarette consumption: nonsmokers, smokers of up to one-half pack per day, and smokers of more than one-half pack per day. Though broad, each category is quite homogeneous with regard to bladder cancer risk.

Whether controlled for cigarette smoking or not, *all* risk estimates are controlled for age. This was done despite the rigid age-match because, within small comparison groups, differences between the ages of cases and controls could have occurred. Three groupings were used in controlling for age: 20–59, 60–74, and 75–89. It can be demonstrated that—in terms of occupational opportunities—no meaningful age differences exist between cases and controls in any of the age- and smoking-specific subgroups used in the control procedures.

For descriptive purposes only, observed and "expected" numbers of cases are presented. The expected numbers result when the cases are distributed with respect to occupation as are the controls. All expected numbers are controlled for age as are the risk estimates and, when specified, for cigarette smoking as well. Most of the relative risks and their 95% confidence limits were derived using Sheehe's[23] modification of Woolf's technique. It is pointed out that, in minimizing bias, Sheehe's procedure leads to a conservative estimate of the relative risk. Those estimates of relative risk and confidence limits associated with a descriptive expected value of 5 or less have been computed using the asymptotic maximum likelihood method described by Gart.[12] Based on either technique, if the confidence limits do *not* include 1.00 the risk is "statistically significantly" different from that of the comparison group with a probability due to chance of less than 5%.

## RESULTS

Table 1 shows the completeness of the occupation histories and the comparability of cases and controls. None of the differences is statistically significant, and it appears that the groups had quantitatively similar working lives and provided interviews similar in quality. The analyses presented are restricted to men; reference to women is made at the conclusion of this section.

### Exposure Classification

*Relative risks:* Observed and expected numbers of case occupations in each exposure code category can be seen in Table 2. The first set of expected numbers is controlled for age-group; the second set is controlled both for age and cigarette smoking. The two sets of expected numbers are quite similar, implying that smoking is not a confounding factor in the association between occupation and bladder cancer. Nonetheless, the relative risks are controlled for cigarette smoking. The risks are relative to a risk of 1.00 for occupations in all the nonsuspect categories combined. For occupations in all the suspect categories combined, the relative risk is 1.29 (95% confidence limits, 1.07–1.56), controlling for age and smoking.

The confidence limits in Table 2 indicate that the relative risk is significantly elevated above 1.00 only for categories 02–rubber and 03–leather. For 3 suspect categories, 01–dyestuffs, 05–paint, and 07–other organic chemicals, risk is elevated but observations are few and statistical significance is not attained. For 3 suspect categories, 04–printing, 06–petroleum products, and 08–other chemicals, no excess risk is demonstrated. If these 3 categories are excluded from the comparison, the relative risk for the remaining "confirmed" suspect occupations is 1.67 (1.30–2.15), controlling for age. Subsequently, the term "confirmed-suspect" refers to occupation categories where both prior information and present findings suggest increased risk, whether or not statistically significant, i.e., categories 01, 02, 03, 05, and 07. Because of this selection, relative risk estimates for these categories as a group are only nominal, even when based on numbers of individuals.

Table 3 presents observed and expected numbers of male cases in each category, each man being categorized once according to his "usual" occupation, the one held longest. The risks are relative to a risk of 1.00 for all men whose usual occupation was in any nonsuspect category. The risks shown in Table 3, with the exception of that for dyestuffs where observations are too few to be meaningful, are quite similar to those in Table 2 and lead to

TABLE 3. Observed and Expected Numbers of Male Cases and Estimates of Relative Risk and the Associated Confidence Limits, According to Category of "Usual" Occupation

| Occupation category* | Male cases | | Rel. risk† | 95% C. L.‡ |
|---|---|---|---|---|
| | Obs. | Exp.** | | |
| Suspect | | | | |
| 01. | 0 | 1.8 | — | 0.00–2.43 |
| 02 | 19 | 11.6 | 1.65 | 0.82–3.35 |
| 03. | 21 | 12.1 | 1.70 | 0.86–3.34 |
| 04. | 5 | 7.7 | 0.75 | 0.29–1.94 |
| 05. | 11 | 8.7 | 1.31 | 0.57–2.97 |
| 06. | 34 | 34.4 | 1.05 | 0.65–1.71 |
| 07. | 3 | 2.0 | 1.62 | 0.32–8.25 |
| 08. | 6 | 6.9 | 0.92 | 0.34–2.46 |
| Nonsuspect | | | | |
| 09. | 25 | 25.7 | 1.00 | — |
| 10 | 29 | 28.4 | | |
| 11. | 5 | 10.5 | | |
| 12. | 125 | 136.4 | | |
| 13. | 62 | 58.8 | | |
| Total men*† | 345 | 345.0 | | |

* As designated in Table 2.
** Controlled for age.
† Relative to a risk of 1.00 for men having a usual occupation in categories 09–13, combined; controlled for age.
‡ 95% confidence limits of the relative risk.
*† Excludes 11 cases and 12 controls with usual occupation indeterminate.

the same categories being selected as "confirmed-suspect." However, the 95% confidence intervals are wider and all include 1.00. Based on usual occupations, the relative risk for all suspect categories is 1.24 (0.89–1.74) and for all confirmed-suspect categories is 1.55 (0.99–2.43), controlling for age.

Table 4 shows observed and expected numbers of male cases *ever* employed in each suspect category. A man is tallied in each suspect category in which he had ever been employed. A man never employed in any suspect category is tabulated in the lowest-numbered nonsuspect category in which he had ever been employed. Again, to show that cigarette smoking is not responsible for an indirect association of bladder cancer risk with occupation, 2 sets of expected values are presented, one of which is controlled for smoking as well as age. The relative risks and the 95% confidence limits presented in Table 4 are also controlled for cigarette smoking as well as age group. The risks in the categories are generally similar to those shown previously, although there is a suggestion of increased risk both in the printing and the petroleum industries. Despite this, we shall not include these two categories among the confirmed-suspect. Based on numbers of men ever so employed, the relative risk for all suspect categories is 1.54 (1.19–1.98) and for all confirmed-suspect categories is 1.84 (1.36–2.50), controlling for age.

Though not demonstrating consistent excess risk, category 06–petroleum products, is nonetheless of interest. This is the largest of the suspect categories, suggesting that it might contain subcategories heterogeneous with respect to bladder cancer risk. In fact, one subcategory, 06.5–machinists and mechanics, accounts for approximately 81% of the observations among controls in category 06 and the relative risk for this subcategory is 0.92. When this group is excluded, other workers with petroleum products have a relative risk of 1.61 (0.93–2.79). It is also interesting that, as reported elsewhere,[4,13,20] risk is appreciably *decreased* for occupations in category 11–farming and ranching, the risk being 0.73 (0.50–1.08) relative to a risk of 1.00 for occupations in *all* categories other than category 11.

Three different estimates have been offered of the relative risk associated with confirmed-suspect catgories. Although based on different units of comparison, these estimates are similar. Based on all occupations, the figure is 1.67

TABLE 4. Observed and Expected Numbers of Male Cases Ever Employed in Each Suspect Occupation Category or in Lowest-numbered Nonsuspect Category, and Estimates of Relative Risk and the Associated Confidence Limits

| Occupation category* | Male cases | | | Rel. risk‡ | 95% C. L.*† |
|---|---|---|---|---|---|
| | Obs. | Exp.** | Exp.† | | |
| Suspect | | | | | |
| 01. | 6 | 4.0 | 3.5 | 2.33 | 0.66–8.24 |
| 02. | 46 | 33.7 | 32.5 | 1.63 | 1.04–2.56 |
| 03. | 65 | 32.7 | 34.3 | 2.25 | 1.46–3.46 |
| 04. | 14 | 13.9 | 15.1 | 1.30 | 0.68–2.49 |
| 05. | 23 | 21.8 | 24.6 | 1.19 | 0.69–2.05 |
| 06. | 79 | 75.3 | 79.0 | 1.18 | 0.82–1.69 |
| 07. | 13 | 10.9 | 9.5 | 1.44 | 0.74–2.80 |
| 08. | 17 | 19.7 | 19.6 | 0.99 | 0.54–1.81 |
| Nonsuspect | | | | | |
| 09. | 40 | 52.4 | 54.9 | | |
| 10. | 46 | 48.5 | 49.1 | | |
| 11. | 13 | 13.8 | 12.1 | 1.00 | — |
| 12. | 102 | 129.6 | 122.1 | | |
| 13. | 13 | 20.7 | 20.7 | | |

* As designated in Table 2.
** Controlled for age.
† Controlled for age and cigarette smoking.
‡ Relative to a risk of 1.00 for men never employed in a suspect occupation; controlled for age and cigarette smoking.
*† 95% confidence limits of the relative risk.

and, based on numbers of men, the figure is 1.55 for those whose usual occupation was so classified and 1.84 for those ever so employed.

*Attributable risks:* To estimate the absolute and attributable[19] risks of bladder cancer associated with occupational exposures, individuals must be used rather than numbers of occupations. Table 5 shows such an analysis, basing the attributable risk on a comparison of annual incidence rates for those ever employed in a confirmed-suspect category with rates for those never so employed. The denominators for the rates are age- and sex-specific estimates of persons in the study area ever and never so employed, based on the distribution of controls. For men between the ages 20–89, those who ever had an occupation within a confirmed-suspect category have an annual bladder cancer incidence rate of 63.7 per 100,000. Men never so employed have a

TABLE 5. Annual Incidence and Attributable Risk per 100,000 and Attributable Risk Per cent According to Age Group for Men and for All Ages for Both Sexes

| Risk measure | Age group, men | | | All ages, 20–89* | |
|---|---|---|---|---|---|
| | 20–59 | 60–74 | 75–89 | Men | Women |
| 1. Confirmed-suspect,† incidence | 22.5 | 188.5 | 284.5 | 63.7 | 19.7 |
| 2. All other, incidence | 11.4 | 87.7 | 217.5 | 34.4 | 12.7 |
| 3. Total population, incidence | 14.9 | 111.0 | 233.0 | 41.8 | 13.5 |
| 4. Confirmed-suspect, attrib. risk | 11.1 | 100.8 | 67.0 | 29.3 | 7.0 |
| 5. Population, attrib. risk | 3.5 | 22.3 | 15.5 | 7.4 | 0.8 |
| 6. Population, attrib. risk per cent | 23% | 20% | 7% | 18% | 6% |
| 7. Relative risk‡ (95% C. L.) | 1.97 | 2.15 | 1.31 | 1.84(1.36–2.50) | 1.55(0.75–2.35) |
| 8. Total cases | 127 | 226 | 138 | 491 | 177 |

* Adjusted by direct method to the age distribution of all men and women, respectively, in the study area aged 20–89.
† Incidence rate among persons who ever held an occupation in a confirmed-suspect category (01, 02, 03, 05, and 07 in Table 2).
‡ Relative to a risk of 1.00 for persons who never held a confirmed-suspect occupation.

rate of 34.4. The difference between these rates, 29.3 cases per year per 100,000 men ever so employed, is the attributable risk of occupational hazards among the exposed. The male population as a whole has an annual incidence rate of 41.8 cases per 100,000 men. The difference between this rate and that of the unexposed is the attributable risk of occupational hazards among the adult male population. This figure 7.4 cases per 100,000 men per year or about 18% (7.4 × 100%/41.8) of the bladder cancer experience of men in the study area, is the amount of disease attributable to the population's employment experience in confirmed-suspect occupation categories. This is probably a conservative estimate of the total impact of occupational exposures since there may be other hazards not reflected in the confirmed-suspect categories.

Age-specific data in Table 5 suggest that among elderly men the number of cases attributable to occupation is small. Only 7% of the 138 cases in the 75–89 age range are likely to be so caused as compared with about 21% of the 353 cases in the 2 younger age groups. Table 5 also shows attributable risk figures for women, all ages 20–89. Age-specific data are not shown for women, since each such estimate is based on few observations and is unstable.

Table 6 shows estimates of absolute and attributable risks comparable to those in Table 5. All rates shown are based on numbers of men but the basis of classification (ever employed or usual occupation) and the definition of "exposure" (confirmed-suspect or all suspect categories) differ between columns. Comparison of the estimates of the population-attributable risks given in Tables 5 and 6 shows that this quantity is identical for both definitions of exposure. This must be so, since the confirmed-suspect categories include all occupations in which excess risk was actually observed and the figure is not increased by including categories where no excess risk is demonstrated. The quantity does change appreciably, however, with change in the basis of classification. With "usual" occupation as the basis of classification, the attributable risk for men is as low as 3.0 cases per 100,000 per year or 7% of male bladder cancer. The higher estimates of 7.4 cases and 18%, based on men ever employed in a confirmed-suspect occupation, are probably more valid. The duration of occupational exposure adequate to increase risk is probably 2 years or less.[8,22] This is much shorter than the average length of usual occupations in this study, 34 years. The discrepancy between the estimates emphasizes the need for lifetime occupation histories if the full impact of occupational exposures is to be revealed.

TABLE 6. Annual Incidence Rates and Attributable Risk per 100,000 and Attributable Risks Per cent for Men, According to Several Bases of Classification and Definitions of Exposure

| Risk measure | All ages, 20–89* | | |
|---|---|---|---|
| | A | B | C |
| 1. Exposed.† incidence | 51.5 | 50.5 | 67.8 |
| 2. Unexposed. incidence | 34.4 | 38.8 | 38.8 |
| 3. Total, incidence | 41.8 | 41.8 | 41.8 |
| 4. Exposed, attributable risk | 17.1 | 11.7 | 29.0 |
| 5. Population, attributable risk | 7.4 | 3.0 | 3.0 |
| 6. Population, attributable risk per cent | 18% | 7% | 7% |
| 7. Exposed, relative risk‡ | 1.50 | 1.21 | 1.75 |

* Age-adjusted, as in Table 5.

† Incidence rate among men who:
A—Were ever employed in any suspect category (categories 01-08 in Table 2).
B—Had their usual occupation in any suspect category.
C—Had their usual occupation in any confirmed-suspect category only.

‡ Relative to a risk of 1.00 among all men who do not qualify as "exposed" in the respective columns.

*Age:* Association of a disease with occupational exposure is supported if the exposed cases are younger than the unexposed. A basic assumption is that the age distribution of the exposed and the nonexposed populations are similar. The data on controls suggest that the assumption is valid for men in the study area. Controls ever employed in a confirmed-suspect occupation had a mean age of 65.8 ± 1.2 (standard error) years and those never so employed were nearly identical, 65.7 ± 0.8 years. However, cases ever employed in a confirmed-suspect occupation had a mean age of 65.6 ± 1.0 years while cases never so employed had a mean age of 66.9 ± 0.9 years. While exposed cases are somewhat younger, 1.3 years, than those never exposed, the difference is not statistically significant.

*Non-bladder cases:* Twenty-one (6%) of the male cases had lower urinary tract cancer not involving the bladder. These men are similar to the bladder cancer cases in mean age, 68.8 vs. 66.3 years, mean number of occupations, 3.6 vs. 3.5 and history of leather working, 7 occupations observed, 2.6 expected. In the rubber industry, there were 2 occupations observed and 2.2 expected, while, in petroleum products, there were 9 observed and 6.2 expected. Expected values are less than 2.0 in

other suspect categories. These 21 men also have a cigarette-smoking experience similar to that of the true bladder cases.[9] No conclusion is reached, but it is suggested that transitional and squamous-cell cancers of the lower urinary tract compose a single disease entity, etiologically, irrespective of involved site.

### Title Classification

Table 7 shows relative risks for those occupation titles which are most comparable to the suspect exposure categories. In addition, risk estimates are provided for those titles suggested by previous investigators to convey increased risk and for all other titles where the relative risk exceeds 1.20 and is based on an expected value of at least 10.0 occupations. Risks are relative to a risk of 1.00 for occupations in all title codes. The title classification supports the exposure classification with respect to the rubber, leather, and paint industries. Indeed, the relative risks for these industries are similar as estimated by either classification system. Excess risk in dyestuffs is not supported by the title code, but there was only one occupation so classified among the cases and none among the controls. Risk for workers in organic chemicals can not be evaluated by the title code which does not separate subgroups of chemical workers. As was true for the exposure code, the title code shows no increased risk for occupations in the printing, petroleum, or chemical industries. However, the title code for petroleum workers, like the corresponding exposure category, may be so inclusive as to mask increased risk among subgroups.

The present data do not support suggestions that bladder cancer risk may be increased among tailors, pressers, barbers, sailors, and deckhands, or workers with metal or wood. However, for none of these groups is the number of observations adequate to exclude the possibility of increased risk. The title code newly identifies several occupation groups which may be at excess risk. It is cautioned that these groups (cooks, construction workers, shipping clerks, postal clerks, and other clerical workers) suggested themselves *a posteriori* from among the 42 title code designations.

When the title code expected values were controlled for cigarette smoking, the relative risk among rubber workers increased to 2.06. Among other title groups comparable to the exposure categories, the risks were essentially unchanged. After controlling for cigarette smoking, the risks among those groups newly identified by the title code were: cooks, 1.73; construction workers, 1.13; shipping clerks, 1.50; postal clerks, 1.27; other clerical workers, 1.38. For none of these groups is the relative risk significantly greater than 1.00 before or after controlling for cigarette smoking.

TABLE 7. Observed and Expected Numbers of Occupations among Male Cases and Estimates of Relative Risk, by Occupation Title

| Occupation Title | Male case occupations | | Relative Risk† |
|---|---|---|---|
| | Obs. | Exp.* | |
| Dyestuffs-laborer | 1 | 0.0 | — |
| Rubber-foreman, laborer | 31 | 18.4 | 1.68 |
| Leather-foreman, laborer shoemaker, repairer | 63 | 34.5 | 1.83 |
| Printer | 7 | 12.9 | 0.54 |
| Painter | 21 | 14.8 | 1.42 |
| Petroleum worker | 80 | 83.7 | 0.96 |
| Chemical worker | 12 | 17.9 | 0.67 |
| Tailor, presser‡ | 8 | 7.0 | 1.14 |
| Barber‡ | 4 | 7.2 | 0.56 |
| Fisherman, sailor, deckhand‡ | 26 | 33.1 | 0.79 |
| Metal worker‡ | 26 | 30.8 | 0.84 |
| Carpenter, wood worker‡ | 22 | 20.2 | 1.09 |
| Cook, kitchen and counter worker | 32 | 20.7 | 1.55 |
| Construction worker | 73 | 60.1 | 1.21 |
| Shipping, stock clerk | 33 | 23.5 | 1.40 |
| Postal clerk, mail carrier | 18 | 12.0 | 1.50 |
| Other clerical workers | 19 | 15.3 | 1.24 |
| Others | 765 | 828.9 | — |
| Total occupations | 1241 | 1241.0 | 1.00 |

* Controlled for age.
† Relative to a risk of 1.00 for all occupations.
‡ Included because others have suggested these may be risk occupations.

### Women

Data on women are limited because bladder cancer is uncommon among them and because they have less industrial experience than men. About 60% of female control and 51% of case occupations were coded 12.8 (service occupation—no exposure likely) on the exposure code, largely reflecting status as "housewife." As classified by the exposure code, in the rubber industry there were 6 occupations observed and 3.5 expected; in the leather industry, there were 8 observed and 6.7 expected; among all other confirmed-suspect categories there were 3 occupations observed and 2.6 expected. As classified by the title code, and controlling for cigarette-smoking, there was an excess of occupations in rubber working, 4 occupations observed and 1.7 expected, and

leather working, 7 observed and 5.2 expected. In addition, 31 case occupations were clerical, the expected value being 19.8, a relative risk of 1.83 (1.04–3.22). With this last exception, none of the differences between observed and expected values for women is statistically significant. Although suggested by earlier studies, no excess risk was found for nurses (12 occupations observed, 11.4 expected) or hairdressers (one observed, 0.9 expected).

## Discussion

Previous investigators[11,16,18,27] have emphasized the difficulties of comparing the occupational experiences of 2 groups. We have tried to mitigate these by defining the limits of, and by eliciting, the lifelong experience and by devising 2 independent systems for classifying data, one of which was specifically relevant to bladder cancer.

Results relating to the rubber industry support previous industry-based reports.[7,10,26] As estimated from this study, the relative risk of developing bladder cancer incurred from occupations in this industry is about 1.6. This is similar to the mortality ratio of 164 found by Case and Hosker[7] for male rubber workers in England and Wales from 1936 to 1951. It is lower than other estimates of risk appearing in the same report and later figures.[6] Although meticulous, the early study[7] of rubber workers was not the detailed epidemiologic inquiry which Case initially recommended and subsequently urged.[6,7] Indirect data sources were used and specific hazards in the industry were not identified. Reasonably, however, the suspect naphthylamine-containing antioxidant which had prompted the study was incriminated. Use of this antioxidant was discontinued by the British rubber industry in 1949. However, in 1967–1968, death certificates of rubber workers in England and Wales continued to mention bladder tumor about 3 times as often as expected.[6] It is not known when or to what extent rubber manufacturers in the United States discontinued use of the suspect antioxidant. Possibly, the current excess risk in the rubber industry in the United States, and that in England and Wales as well, represent the effects of hazardous exposures sustained as long as 20 years ago. On the other hand, there may be continuing hazardous exposures in both countries.

The present results indicate increased risk of bladder cancer in the leather and leather products industries. No such association was found among a large series of cases of bladder tumor assembled in Leeds, England.[2] Nonetheless, 2 early studies[14,25] suggested, and 2 more recent reports support, the association of leatherworking and increased bladder cancer risk. Lockwood's investigation[18] of prevalent bladder cancer cases in Copenhagen in the late 1950's indicated possible increased risk for workers in "skins, leather and rubber," 5 cases observed and 1.6 expected. In a study done in New York City, at about the same time, Wynder et al.[27] found that 12 cases, but only 3 controls, had held "long term jobs" involving shoes or leather. Their data indicated a "higher risk for shoe repairers but not for shoemakers."

An idea of the hazardous exposures among leather workers is given in Table 8. Most excess cases are found in subcategories 03.3–03.4—finishing and associated processes, comprised of occupations which involve cutting

TABLE 8. Observed and Expected Numbers of Male Cases Ever Employed in Category 03–Leather-Leather Products, According to Lowest-numbered Subcategory and Estimates of Relative Risk and the Associated Confidence Limits

| | | Male cases | | | |
|---|---|---|---|---|---|
| | Occupational subcategory | Obs. | Exp.* | Rel. risk† | 95% C. L.‡ |
| 03.1–03.2 | Preliminary processes and tanning | 8 | 7.1 | 1.45 | 0.68–3.10 |
| 03.3–03.4 | Finishing and associated processes | 44 | 17.3 | 2.65 | 1.57–4.47 |
| 03.7–03.9 | Contact with finished product. Exposure type uncertain | 13 | 8.1 | 1.73 | 0.89–3.36 |
| | Total men | 65 | 32.5 | — | — |

* Controlled for age and cigarette smoking.
† Relative to a risk of 1.00 for men never employed in a suspect occupation. Controlled for age and cigarette smoking.
‡ 95% confidence limits of the relative risk.

and assembling leather pieces and related activities, e.g., buffing. Acheson et al.[1] found increased risk of nasal cancer among finishing room workers in the leather boot and shoe industry in England. These men are exposed to leather dusts, and it is plausible that a single absorbable carcinogen may cause tumors both at the site of contact, the upper respiratory tract, and the site of excretion, the urinary tract.

Association of bladder cancer risk with dyestuffs manufacture was not found in the present investigation, but this does not contradict earlier positive studies; the industry has never been prominent in the study area. The data suggest little increased risk in the chemical industry, possibly restricted to workers with organic chemicals. This is consistent with the report of only a slight excess of deaths due to bladder cancer, 26 observed and 21 expected, among members of the American Chemical Society.[17]

The amount of bladder cancer attributable to occupational exposures might be expected to vary between populations, reflecting their differing occupational experiences. However, there are no previous estimates of this value available for comparison with the present findings. Though not strictly comparable, 2 estimates of a population's occupation attributable risk *per cent* have been made and may be compared with the present estimate of 18%. One estimate was based on all male deaths occurring between 1965 and 1968 in a highly industrialized county borough in England.[26] There were 49 deaths in which bladder tumor was mentioned on the death certificate. By detailed inquiry, a "potentially significant" occupation history was found for 33% of these men, but no comparable history was ascertained for unaffected persons. The figure of 33%, therefore, represents a maximum estimate of the male population's attributable risk per cent of bladder cancer, at least for the occupations considered significant. In the Leeds study, it was considered that approximately 23% of the male cases might be attributable to occupational experiences.[3] This figure is not strictly referrable to "a population" since a series of prevalent, not incident, cases was used. However, the 3 estimates are quite consistent with one another and reveal the size of the problem of occupation-induced bladder cancer. Case's suggestion[6] that, among men in England and Wales, about 1% of bladder tumor deaths may be due to occupational exposures is clearly too low. Yet, even among men in industrialized societies, probably not more than one fourth of the disease can be attributed to occupational exposures.

The few data available for women allow no conclusions. Nonetheless, according to both classification schemes, the observed-expected differences are in the same direction as those for men. The data do imply that occupational exposures can not account for any significant amount of bladder cancer among women in the study area.

The title code has indicated two occupation groups that warrant further investigation: cooks—counter workers, and clerical workers. Increased bladder cancer risk among male clerical workers has been reported previously, based on United States mortality data.[13] In the present study, the finding appears in both sexes and is statistically significant among women. However, neither cooks nor clerical workers are exposed to any known carcinogen in their work. The possibility that some etiologic factor is associated with the life style of persons in these occupations must be kept in mind. Furthermore, since the groups suggested themselves *a posteriori*, independent validation is required before it is concluded that the groups are in fact at increased risk.

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