

## Letters to the Editor

The Editors of the Journal of the National Cancer Institute solicit for publication letters pertaining to recent articles that have appeared in the Journal. It is our opinion that this exchange of comment and ideas relevant to current research will serve as a further means of good communication. Letters submitted for publication should not be considered a method of introducing new data to the reader, but should contribute meaningful and constructive discussion to those papers that have been published. The author of a paper mentioned in a letter will be given the opportunity of replying in print to comments prior to publication of any correspondence. The decision to publish a letter and the editing of all published correspondence will be the prerogative of the Board of Editors, subject to approval by the correspondents.

### Comments On:

Tumors of the Urinary Bladder: An Analysis of the Occupations of 1,030 Patients in Leeds, England, by Honor M. Anthony and Gretta M. Thomas, *Department of Experimental Pathology and Cancer Research, School of Medicine, University of Leeds, Leeds, LS 2 9NL, England.*—*J Nat Cancer Inst* 45:879-895, 1970.

To the Editor:

The authors of the above paper suggest that having had only one occupation in a working lifetime is a meaningful risk factor in bladder cancer; they estimate that about 18% of the bladder tumors in their series could be attributed to such exposure. We would like to raise two points.

1) The above conclusion derives from table 9, the relevant data from which are presented in our table 1. The figure of 18% (the difference between 53 and 35%) assumes that the "expected" value in the upper left cell of the table is 35%. That is, it is assumed that all patients had the same likelihood of exposure to a single occupation as did the controls. The assumption is wrong and the estimate of 18% is too low. If having had a single occupation is associated with increased risk (and the table shows that this is so), then some patients necessarily had to be so exposed and the 35% probability applies only to the remainder. We believe the correct percentage as based on these data is 27%; this can be shown as follows:

The 53% of patients in the upper left cell of table 1 may be thought of as comprised of two groups. The first group ( $x$ ) is the group in question, the excess over the expected value. Since these persons are defined as in excess of the expected value, they must have had only one occupation. There is no probability that they could lie outside this cell. The second group consists of all the other patients who appear in the cell due to chance alone. This is equal to all the remaining patients  $(1.00 - x)$  multiplied by the same probability of being exposed as is seen among the controls, *i.e.*, .35. Thus the percentage of patients "expected" in the cell is  $.35(1.00 - x)$ . The relationship is described as follows:

$$.53 = x + .35(1.00 - x)x = .27$$

TABLE 1.—Percentage of persons by number of occupations recorded (war service excepted)

Number of occupations	Bladder tumor patients (%)	Surgical controls (%)
1	53	35
2+	47	65
Total	100	100

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The difference between 18 and 27% is not overwhelming, but the general point is that the higher the proportion exposed among the controls, the greater the error in the estimate. Typical data on lung cancer and cigarette smoking (1) illustrate the problem clearly. Reading left to right, top to bottom, the percentages that would appear as in table 1 are 97, 78, 3, and 22%. If we do as Anthony and Thomas have done and subtract 78 from 97, we might suggest that about 19% of lung cancer could be attributed to smoking. However, using the method in the example above we would arrive at an estimate of 86%, quite consistent with a direct estimate of about 89% (2).

2) It seems curious to designate a lifetime of "one occupation" as a meaningful exposure. It is probably true (3, 4) that industrial exposures of 2 years or less increase risk. In addition, risk is at a maximum for occupations held for intermediate durations (10-20 years) and falls thereafter, at least among dye workers (3). To estimate the percent of disease that is likely to be due to occupation in this series, we suggest using the data in the authors' table 4, which deals with subgroups of occupations "with consistently increased relative risks." For the matched-pairs group this table may be condensed to our table 2. Using the method described above, one can estimate what we would term "the attributable risk percent" for this series as 19%. It is entirely coincidental that this approximates the original percentage suggested by the authors. It may, or may not, be coincidental, however, that it approximates our own estimate (5) of 18% for eastern Massachusetts.

TABLE 2.—Numbers of patients and controls exposed or not exposed to occupations in orders with consistently increased relative risks—predominant occupation

	Patients	Surgical controls
Exposed	148	103
Not exposed	192	237
Total	340	340

## REFERENCES

- (1) DOLL R, HILL AB: A study of the aetiology of carcinoma of the lung. *Brit Med J* 2:1271-1286, 1952
- (2) ———: Mortality in relation to smoking: Ten years'

observations of British doctors. *Brit Med J* 5395: 1399-1410, 1460-1467, 1964

- (3) CASE RA, HOSKER ME, McDONALD DB, et al: Tumours of the urinary bladder in workmen engaged in the manufacture and use of certain dyestuffs intermediates in the British chemical industry; role of aniline, benzidine, alpha-naphthylamine, and beta-naphthylamine. *Brit J Industr Med* 11:75-104, 1954
- (4) SCOTT TS: *Carcinogenic and Chronic Toxic Hazards of Aromatic Amines*. New York, Elsevier Publishing Co., 1962
- (5) COLE P, HOOVER R, FRIEDEL GH: Occupation and cancer of the lower urinary tract. Submitted for publication.

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To the Editor in Reply to Comments of Cole and Hoover:

The correction of the estimate of the proportion of men present in our series because of having had one occupation only suggested by Cole and Hoover is clearly valid. The corrected estimate is, therefore, 27%, giving a total of 30% for men present because of occupational hazard when the short-term dye hazard risks are included.

However, Cole and Hoover seem not to have appreciated the fact that two patterns of industrial risk are apparent in our findings. One pattern exhibits the characteristics noted in their point 2, and is shown by dyeworkers, and possibly also by hairdressers and tailors' cutters. The other pattern is of long-term risk only, shown up by excess in predominant occupation and in 20 years+ but not in any other groups. This pattern was seen in most other suspect occupations, particularly among tailors' pressers, and textile workers. Only the second type of risk could be held to contribute to the excess of bladder tumor patients who had had one occupation only.

It is possible to calculate the industrial risk as they suggest, from table 4, though their figures are

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an underestimate as they take no account of the medical subgroup of professional workers, and the figures might be better amended to read 147, 97, 193, 243, giving an attributable risk of 21%. It is possible to do the same for the 519 Leeds men patients, using the "expected" levels from census figures and adjusting for a diminishing total of men not apparently at risk until the figure stabilizes. Including all predominant occupations with consistently increased relative risk, this occurs at an attributable risk figure of 14.3%. Both these calculations are based on figures for predominant occupation, which show only 1.2% of the whole series as engaged in dye works, whereas 3% of the whole series had been so engaged at some time in their lives (table 7). Both figures are, therefore, 2% too low.

The fact that calculations based on occupations with consistently increased relative risks give figures lower than those based on the numbers having had one occupation only suggests to us that there may be other long-term industrial hazards in this area which we were not able to detect.

It is interesting that Cole, Hoover, and Friedell have found a closely similar attributable risk in their series, but in the different industrial circumstances it is probably, as they say, coincidental.

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