Risk factors for kidney cancer in New South Wales. IV. Occupation

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Abstract

In a population based case-control study of kidney cancer in New South Wales, data from structured interviews with 489 cases of renal cell cancer (RCC), 147 cases of renal pelvic cancer (CaRP), and 523 controls from the electoral roles were obtained about employment in certain industries or occupations, and exposure to particular chemicals chosen because of suspected associations with kidney cancer. A low level of education increased the risk for CaRP but not RCC. After adjustment for known risk factors, exposure to asbestos significantly increased the risk for RCC (relative risk (RR) = 1·62; 95% confidence interval (95% CI) 1·04–2·53). Working in the dry cleaning industry had a stronger link with CaRP (RR = 4·68; 95% CI 1·32–16·56) than with RCC (RR = 2·49; 95% CI 0·97–6·35). Working in the iron and steel industry doubled the risk for CaRP (RR = 2·13; 95% CI 1·04–4·39) whereas employment in the petroleum refining industry had a non-significant association with CaRP (RR = 2·60; 95% CI 0·88–7·63) and none with RCC.

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Despite the variety of industries concerned (dyeing, rubber and tyre manufacture, electrical and leather industries), the basis of occupationally induced urothelial cancers (bladder, renal pelvis, and ureter) is essentially known and understood—the implicated chemicals are for the most part aromatic amines for which a recognised mechanism exists.[1] By contrast, none of the occupational risks postulated for cancer of the renal parenchyma (renal cell cancer (RCC)) have been found consistently in population based studies.[2–15]

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The risk for RCC associated with working in specified industries or with occupational exposure to particular chemicals (chosen because of suspected associations with kidney cancer) has been examined in an international collaborative population based case-control study coordinated by the US National Cancer Institute. The participating centres, either in areas of high incidence of RCC or with a particular interest in kidney cancer, were in the United States (Minnesota), Denmark, Sweden, Germany (two centres), and Australia (New South Wales). The analysis of results from New South Wales pertaining to these factors are presented here together with findings for cancer of the renal pelvis.

Methods

Potential cases comprised all incident cases in 1989–90 of cancer of the renal parenchyma (ICD–9 189·0) and renal pelvis (ICD–9 189·1) in residents of New South Wales who were aged 20–79 at diagnosis; control subjects were selected from the electoral rolls using proportional random sampling based on the expected age distribution of the cases. The study population was confined to subjects whose names were in a current electoral roll, whose telephone number could be found, and who could speak English.

Cases were identified through statutory notification to the New South Wales Central Cancer Registry by hospitals, pathology laboratories, and radiotherapy departments[16] as well as by regular contact with urologists throughout New South Wales. Up to 31 July 1991 (allowing for late notifications) 744 eligible cases of RCC and 200 of CaRP were identified. Permission was requested from the attending doctor for inclusion in the study, followed by a letter to the case seeking participation. The release of information from the Cancer Registry was conditional upon adherence to a strict protocol that did not permit repeated approaches to either the doctor or the patient; nor could information be obtained from relatives of the patients. For RCC, loss of cases due to death (23%), refusal (doctor 2%, patient 1%), or non-response (doctor 1%, patient 5%) resulted in a case group comprising 322 men and 181 women. For CaRP, 59 men and 90 women were interviewed.

Death (15%), refusal by doctor (1%) or patient (5%), and non-response by doctor (3%) or patient (2%) accounted for the rest. In each of the 12 five year age groups between 20 and 79, the percentages of the potential RCC cases who participated were 80, 100, 83, 77, 79, 78, 75, 79, 74, 65, 55, and 47 respectively. For CaRP, the percentages who participated in the nine five year age groups between 35 and 79 were 100, 100, 89, 89, 84, 90, 74, 58, and 59.

The diagnosis of interviewed cases was based on histopathology of the kidney (87% RCC, 92% CaRP) or other tissue (1% RCC), fine needle aspiration cytology of the kidney (4% RCC), or by computerised tomography, ultrasound, or contrast radiography (8% of each).

Of the proportional random sample obtained from the current New South Wales electoral rolls, telephone numbers were found for 803. An initial letter seeking participation was followed up, if necessary, by a second letter and up to 10 telephone calls. The information on the rolls was out of date for 60 subjects (52 moved, eight dead) and 18 could not speak English. Of the remaining 725, 74% were interviewed, the rest comprising refusals (no reason 16%, ill health 7%, other reason 2%, senility <1%) and non-respondents (2%). Among men, the proportions of interviewed controls in each 10 year age group were not significantly different from those of the non-respondents ($\chi^2 = 1{\cdot}03$, df = 3, p = 0·79) but the women who were not interviewed were slightly older than those who were (65 (SD 8) *v* 62 (SD 9) years, t = 3·092, df = 389, p < 0·001).

One trained interviewer carried out all the interviews between May 1989 and July 1991. All but 10 of the cases (seven RCC, three CaRP) were interviewed within one year of diagnosis (55%, 87%, and 96% within three, six, and nine months of diagnosis respectively). Face to face interviews were held in the homes of all subjects who lived in the Sydney Metropolitan area (256 RCC, 71 CaRP, 232 controls). For subjects living in the rest of New South Wales (233 RCC, 76 CaRP, 291 controls), the checklists to be used with the standard questionnaire were mailed with a request to keep them unopened but accessible for a subsequent telephone interview. Self administered questionnaires were completed by 14 RCC cases, two CaRP cases, and 12 controls as this was the only means by which these subjects would participate.

The questionnaire (core questions identical with those used in the other collaborating centres) sought information about employment in certain industries and occupations and exposure to particular chemicals chosen because of suspected associations with kidney cancer, as well as data about other suspected risk factors and confounders. Demographic data including years of formal schooling and whether or not subjects had received technical or vocational training or attended university were also requested.

Analysis

Initial evaluation included inspection of frequencies of the variables. As the 28 self administered questionnaires contained an unacceptably high level of missing data, it was decided to restrict the analysis to the 489 cases and 523 controls who were interviewed either face to face or by telephone. Tertiles of exposure variables were calculated on the basis of their distribution in the entire control group; tertiles for age were based on cases and controls combined.

Relative risks (RRs), together with 95% confidence intervals (95% CIs), were estimated from

Table 1 Characteristics of cases and controls for age, marital state, and education, New South Wales, 1989–90

	Population controls		*Renal cell cancer*		*Renal pelvic cancer*	
	Men (n=231)	*Women (n=292)*	*Men (n=310)*	*Women (n=179)*	*Men (n=58)*	*Women (n=89)*
Age (y):						
20–29	0	0	2 (0·6%)	3 (1·7%)	0	0
30–39	6 (2·6%)	7 (2·4%)	13 (4·2%)	3 (1·7%)	3 (5·2%)	0
40–49	26 (11·3%)	20 (6·8%)	43 (13·9%)	24 (13·4%)	6 (10·3%)	3 (3·4%)
50–59	54 (23·4%)	80 (27·4%)	68 (21·9%)	52 (29·1%)	7 (12·1%)	17 (19·1%)
60–69	87 (37·7%)	102 (34·9%)	116 (37·4%)	58 (32·4%)	27 (46·6%)	41 (46·1%)
70–79	58 (25·1%)	83 (28·4%)	68 (21·9%)	39 (21·8%)	15 (25·9%)	28 (31·5%)
Marital state:						
Ever married	222 (96·1%)	281 (96·2%)	292 (94·2%)	169 (94·4%)	55 (94·8%)	87 (97·8%)
Educational level:*						
≤6 years at school	13 (5·6%)	26 (8·9%)	18 (5·8%)	17 (9·5%)	5 (8·6%)	7 (7·9%)
7–10 years at school	53 (22·9%)	115 (39·4%)	82 (26·5%)	71 (39·7%)	19 (32·8%)	55 (61·8%)
≥11 years at school	14 (6·1%)	20 (6·8%)	21 (6·8%)	9 (5·0%)	2 (3·4%)	2 (2·2%)
Vocational or technical training	120 (51·9%)	119 (40·8%)	164 (52·9%)	73 (40·8%)	31 (53·4%)	23 (25·8%)
University degree	31 (13·4%)	12 (4·1%)	25 (8·1%)	9 (5·0%)	1 (1·7%)	2 (2·2%)

*Mutually exclusive categories; subjects allocated to highest level for which they qualify.

Table 2 Risk ratios for kidney cancer associated with certain occupations, New South Wales, 1989–90

Employment in/as	*Population controls (n=523) No exposed*	*Renal cell cancer (n=489)*		*Renal pelvic cancer (n=147)*	
		No exposed	*RR* (95% CI)*	*No exposed*	*RR† (95% CI)*
Petroleum refining industry	11	15	1·01 (0·45–2·25)	8	2·97 (1·10– 8·02)
Blast furnaces and coke ovens	23	36	1·24 (0·71–2·16)	9	1·89 (0·80– 4·46)
Iron and steel industry	39	52	1·18 (0·75–1·85)	19	2·39 (1·26– 4·52)
Dry cleaning industry	7	16	2·70 (1·08–6·72)	8	6·09 (1·95–18·90)
Printing or graphics industry	24	29	1·18 (0·67–2·08)	6	0·82 (0·32– 2·11)
Machinist or tool maker	34	48	1·15 (0·72–1·86)	16	1·83 (0·92– 3·61)
Welder	24	40	1·37 (0·80–2·34)	8	1·66 (0·68– 4·03)
Dentist	4	1	0·34 (0·04–3·16)	0	
Physician	7	4	0·48 (0·14–1·70)	0	
Petrol station attendant	32	25	0·69 (0·40–1·21)	9	1·03 (0·46– 2·30)

*Adjusted for age, sex, method of interview, †and education.

multivariate logistic regression by EGRET[17] according to Breslow and Day.[18] All estimates of risk for RCC were adjusted for age (in tertiles), sex, and method of interview. The effect of each factor and of potential interactions were tested by the likelihood ratio test. All factors with a statistically significant influence were included in the final model to estimate the effect of each factor adjusted for all other significant factors.

With case:control ratios of roughly 1:1 for RCC and 1:3·5 for CaRP, the study was big enough to have 90% power to detect an unadjusted RR of about 2·0, given a one sided significance level of 0·05 and 10% of the controls exposed to the risk factor of interest.[18]

Results

Table 1 describes the cases and controls in respect of age, marital state, and educational level. Almost one fifth of RCC cases were aged less than 50 at diagnosis. Cases and controls were similar in the proportions who had ever been married. Although the educational levels achieved were broadly similar between RCC cases and the controls, more male controls had a university degree. Inclusion of a term for education into a logistic regression model (adjusted for age, sex, and method of interview), however, did not indicate an association; nor was there a trend of decreasing risk with increasing level of education. Cases of CaRP were less well educated than controls, and inclusion of a term for education made a significant contribution ($\chi^2 = 6{\cdot}60$, $p = 0{\cdot}01$) to a model also adjusted for two known risk factors—namely, cigarette smoking,[19] and analgesics containing phenacetin.[20]

Table 2 gives the numbers of subjects answering yes to the series of questions "Have you ever been employed in the (named) industry, or as a (named occupation)?" It also gives an adjusted risk ratio for each type of cancer. Similarly, table 3 presents responses to the question "Were you ever exposed to (material) while working on a job that you held for one year or longer?" Significantly raised RRs were found for the dry cleaning industry (both types of cancer), the iron and steel industry (CaRP), the petroleum refining industry (CaRP), and exposure to asbestos (RCC), solvents (RCC), cutting oils or mists (RCC), or other petroleum products (both types of cancer). When these factors were adjusted for each other and for known risk factors for RCC or CaRP, however (table 4), most associations were no longer significant.

ASBESTOS

Exposure to asbestos significantly increased the risk

Table 3 Risk ratios for kidney cancer associated with occupational exposures, New South Wales, 1989–90

Exposure to	*Population controls (n=523) No exposed*	*Renal cell cancer (n=489)*		*Renal pelvic cancer (n=147)*	
		No exposed	*RR* (95% CI)*	*No exposed*	*RR† (95% CI)*
Asbestos	37	70	1·58 (1·02–2·44)	11	1·24 (0·58–2·65)
Solvents	78	109	1·54 (1·11–2·14)	24	1·40 (0·82–2·40)
Petrol	48	53	1·23 (0·81–1·86)	17	1·31 (0·70–2·46)
Cutting oils or mists	28	51	1·99 (1·23–3·23)	11	1·66 (0·76–3·62)
Other petroleum products	39	64	1·96 (1·28–2·99)	20	2·16 (1·44–4·08)
Insecticides or pesticides	40	48	1·39 (0·89–2·18)	8	0·70 (0·31–1·58)
Herbicides	30	38	1·45 (0·87–2·40)	6	0·83 (0·33–2·10)
Radiation or radioactive material	21	15	0·70 (0·35–1·39)	2	0·56 (0·12–2·52)
Cadmium	9	10	1·13 (0·45–2·82)	4	2·59 (0·73–9·17)

*Adjusted for age, sex, method of interview, †and education.

Table 4 Occupational risk factors for kidney cancer, New South Wales, 1989–90

	Renal cell cancer	*Renal pelvic cancer*
	RR (95% CI)*	*RR† (95% CI)*
Exposure to asbestos	1·62 (1·04–2·53)	—
Dry cleaning industry	2·49 (0·97–6·35)	4·68 (1·32–16·56)
Iron and steel industry	—	2·13 (1·04– 4·39)
Petroleum refining industry	—	2·60 (0·88– 7·63)

*Adjusted for age, sex, method of interview and cigarette smoking, and *body mass index or †education and phenacetin containing analgesics.

for RCC by a factor of 1·6 (table 4), a link seen more clearly among men (RR = 1·73, 95% CI 1·04–2·89; 64 cases, 32 controls) than women (RR = 1·17, 95% CI 0·30–4·55; five cases, five controls). With simultaneous adjustment for duration of exposure and year exposure began in a logistic model including only subjects who had ever been exposed to asbestos, the risk for RCC was fivefold higher in those whose exposure began after rather than before 1956 (table 5).

DRY CLEANING INDUSTRY

The risk of both types of kidney cancer was increased by working in the dry cleaning industry (table 4), the effect on CaRP (RR = 4·68; 95% CI 1·32–16·56; two male and six female cases, two male and five female controls) being almost twice as great as that for RCC (RR = 2·49; 95% CI 0·97–6·35; eight male and eight female cases).

IRON AND STEEL INDUSTRY

Working in the iron and steel industry doubled the risk for CaRP (table 4). When only subjects who had worked in this industry (17 male, two female cases; 31 male, eight female controls) were considered, simultaneous modelling of tertiles of duration of work (1–5, 6–21, ⩾22 years) and of the year work began in the industry (1930–41, 1942–56, 1957–86) showed no trend in risk for CaRP.

Table 5 Risks of renal cell cancer associated with exposure to asbestos, New South Wales, 1989–90

*Subjects exposed to asbestos**	*No of exposed controls*	*No of exposed cases*	*RR† (95% CI)*
Duration of exposure (y):			
1–3	11	15	1
4–15	11	25	2·23 (0·68– 7·34)
⩾16	14	27	2·09 (0·64– 6·76)
Year exposure began:			
1929–48	14	20	1
1949–55	11	15	1·04 (0·35– 3·09)
1956–86	11	32	5·28 (1·43–19·55)

*Three cases and one control gave no information on period of exposure.
†Model includes both time related exposure variables as well as terms for age, sex, and method of interview.

PETROLEUM REFINING INDUSTRY

A 2·6-fold increased risk for CaRP was linked with the petroleum refining industry (table 4). The small numbers of subjects (eight men with CaRP; nine male and two female controls) reporting this type of work prevented analysis by duration or period of employment. No association was seen with RCC.

Discussion

This Australian study confirms associations between kidney cancer and exposure to asbestos, and work in the petroleum, iron and steel, and dry cleaning industries reported predominantly in North America and Europe.

Support for asbestos as a risk factor for kidney cancer has been provided by cohort studies of workers involved in insulation,[4] production of asbestos,[12] and shipyards (Puntoni *et al* 1979 reviewed by Smith *et al*[21]), each of which showed a significant standardised mortality ratio (SMR) of between 1·7 and 2·7. A case-control study of shipyard workers found an adjusted incidence rate ratio for RCC that remained in the range 1·5–2·0 depending upon the criteria of exposure.[9] Evidence for asbestos fibres reaching the kidney has been furnished by necropsy studies of humans and of rats fed asbestos by gavage; and asbestos fibres have been found in human urine (reviewed by Smith *et al*[21]). Moreover, experimental studies have found asbestos to be a carcinogen for the kidney in the rat.[22] In the present study a link with asbestos was present only in men, the risk ratio of 1·73 being of the same order as those found previously. A higher risk was found in those exposed since compared with before 1956. As litigation seeking compensation for asbestos induced disease has been widely publicised in Australia it is possible that recall bias in this study might explain the association with exposure to asbestos. That the association was found with RCC but not with CaRP indicates a specific, and therefore real, link. The Minnesota case-control study found no association of asbestos with either RCC[5] or CaRP.[23]

A further suspected occupational link with kidney cancer has been exposure to hydrocarbons through work in the petroleum or iron and steel industries. Whereas renal tumours in rats have developed after long term inhalation of gasoline vapours,[24] cohort studies of petroleum industry employees have found no evidence for an increased risk of kidney cancer except perhaps for drivers distributing petroleum products (reviewed by Wong and Raabe[25] and Enterline and Viren[26]), and conflicting findings have emerged from case-control studies.[7 8 10 26] Men working with coke ovens had a higher than expected

mortality from RCC (based on eight deaths) in a cohort study of steel workers[2] whereas case-control investigations of RCC reported contradictory results for exposures defined as petroleum, tar, and pitch products,[5 27] burning coal,[28] and occupational exposure to hydrocarbons.[14] In the present study no association was found between RCC and working in these industries, the increased risk seen for those exposed to other petroleum products and to cutting oils and mists disappearing when adjustment was made in the analysis for other risk factors. By contrast, independent significant twofold raised risks for CaRP were linked with ever being employed in the petroleum industry, and iron or steel industries. Small numbers prevented analysis by duration of employment in the first industry, and no trend was found for the second. Other case-control studies of urothelial cancer, however, also found similar associations; specificially, significantly increased risks for exposure to mineral or cutting oils (RR = 2·8; renal pelvis[23]); coal and coke (RR = 4·0), and asphalt and tar (RR = 5·5; renal pelvis and ureter[29]); and for exposure to benzene (RR = 2·0; mainly bladder[30]).

Suggestions of an increased risk of kidney cancer in the dry cleaning industry (another source of hydrocarbons—for example, Blair 1979, quoted in Blair *et al*[15]) were not confirmed in a recent cohort study of dry cleaning workers.[15] Whereas no association of RCC and organic solvents was found in one small case-control study,[13] an excess risk was found in female dry cleaners in another.[10] Significant fourfold and twofold increased risks for CaRP and RCC respectively were found in the current study; recall bias cannot be ruled out as an explanation.

Although a twofold increased risk of RCC has been attributed to occupational exposure to cadmium,[3] this finding has not been replicated in this or other studies.[5 8 10] Neither could we show a raised risk for RCC among physicians and dentists (the reverse was true) by contrast with the Swedish study linking cancer incidence (1961–79) and census data (1960) that found increased risks among several professional and white collar occupations including physicians and others in the health care industry.[11] A high proportional incidence ratio for RCC has been found in another professional group, architects, in Los Angeles County incidence data for 1972–86.[31] Subjects were not asked about employment in the leather industry so that the possibility of increased risks for RCC[5] as well as CaRP[23 32] could not be determined.

With respect to the educational level achieved, subjects in this investigation resembled those in previous studies of RCC in which only slight differences, if any, were found between cases and controls.[5 8 10 27] By contrast, a greater proportion of cases with CaRP than controls with low educational level was found for both sexes in this and an earlier study in NSW[20] but only among men in the Minnesota survey.[23]

In this study subjects were not asked for a detailed occupational history as the main hypotheses were directed at other possible aetiological factors. Although information was gathered about the most recent and the usual occupation, this was not used in the present analysis, which was based on specific questions relating to industries or exposures under suspicion through other epidemiological studies. Drawbacks of the present investigation include small numbers of exposed subjects, no validation of the self reported exposures, and no possibility of categorising exposures by intensity. Nevertheless, as each of the associations positively identified here has substantial supportive evidence from other studies or known mechanisms of renal or urothelial carcinogenesis, our results do contribute to the overall understanding of occupationally related renal neoplasms.

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