Occupational Kidney Cancer

Exposure to Industrial Solvents

NACHMAN BRAUTBAR, MICHAEL P. WU, ELION GABEL, AND LEE REGEV

University of Southern California School of Medicine, Los Angeles, California 90048, USA

ABSTRACT: We report seven cases of renal cell carcinoma in workers diagnosed with occupational exposure via skin contact and inhalation to industrial solvents containing benzene. The clinical significance of these cases are: (*a*) all seven patients diagnosed with kidney cancer were seen by private physicians who missed addressing occupational history to industrial solvents; (*b*) emphasize the importance of taking an in-depth history including occupational history in any patient presented to the clinician, especially like in these cases, kidney cancer; and (*c*) demonstrate the importance of educating workers. We believe that there exist more patients with renal cancer whose diagnosis has been rendered "idiopathic" due to the lack of detailed occupational, environmental, personal, and family history.

KEYWORDS: renal cell carcinoma; kidney cancer; case reports; benzene; industrial; organic solvents; occupation

INTRODUCTION

Kidney cancer is the general term for malignancies of the kidney. Malignancy of the kidney comprises a heterogeneous class of tumors arising from different cell types within the nephroma. Histopathologic classification of kidney tumors include hypernephroma (renal cell carcinoma), also called nonpapillary cancer, and comprises 75–80% of kidney cancer, papillary renal cell cancer which comprises 10–15%, chromophobe renal cell carcinoma, collecting duct carcinoma, and other unclassified renal cell carcinoma.[1] In the United States, the incidence of kidney cancer is 17 cases per 100,000 person-years and reaches the maximum at the age of 65 years.[2] Kidney cancer is attributed to both genetic and environmental factors. Studies have linked the genetic predisposition of kidney cancer to several conditions, including mutations that lead to Von

Address for correspondence: Nachman Brautbar, 6200 Wilshire Boulevard, Suite 1000, Los Angeles, CA 90048. Voice: 323-634-6500; fax: 323-634-6501.
e-mail: brautbar@aol.com

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Hippel–Lindau syndrome, hereditary papillary renal carcinoma, and tuberous sclerosis Type I and II.[3] Cigarette smoking is a risk factor for kidney cancer. The International Agency for Research on Cancer (IARC) has found sufficient evidence for the carcinogenic role of tobacco smoking in renal pelvis carcinoma.[4] Subsequent epidemiological studies have demonstrated cigarette smoking as a risk factor for kidney cancer. The percentage of kidney cancer attributed to cigarette smoking is between 21% and 30% among men and 9% and 24% among women.[5–7] Diet has been suggested as a risk factor for kidney cancer, however, there is no agreement in the scientific literature.[8] Alcohol is a suspected risk factor, however, it remains only as a possibility. Epidemiological studies associate kidney cancer with excess body weight, overweight, and obesity as measured by the body mass index (BMI).[1] In the United States, obesity attributes 21% of kidney cancer risk.[9] Patients with diabetes also have an increased risk of kidney cancer, mainly those with long-term and uncontrolled diabetes mellitus.[10] Occupational studies have also attempted to address the risk of exposure to asbestos, hydrocarbon, lead, cadmium, and chlorinated industrial solvents.[1]

Many epidemiological studies have investigated the association between solvent exposure and kidney cancer. Case–control studies and cohort studies have been described in the peer-reviewed, scientific literature. TABLE 1 describes selected case–control studies of kidney cancer and exposure to industrial solvents.[11–24] Statistically significant odds ratio (OR) range from 1.2 to 6.4, with some studies controlling for risk factors as age, sex, cigarette smoking, and weight. TABLE 2 summarizes cohort studies that describe exposure to solvents and increased risk of kidney cancer.[25–30]

PATIENTS AND METHODS

We describe here seven patients who were evaluated based on physical examination and review of records, who have developed kidney cancer, and have a history of exposure to industrial solvents. Exposure dose were determined either by job description, material safety data sheets, court records, and/or history of exposure. Although the employers and industry never provided actual levels, based on the collected information, exposures were determined to be substantial. Potential confounding factors are addressed in the "Discussion" section.

RESULTS

The patients studied here have a common denominator of substantial exposure to industrial solvents from 5.5 years to 44 years (average 35 years). TABLE 3 summarizes the seven patients' age, occupation, exposure history and

TABLE 1. Case–control studies of increased risk of kidney cancer and exposure to industrial solvents

Study	Study design	Control group	Exposure	Result	95% CI	Controlled variables
Ref. 11	Death certificate	Noncancer deaths	Petroleum or petrochemicals	OR = 2.27	1.01–5.43	—
Ref. 12	Interviews	Other cancer sites	Aviation gasoline	OR = 2.6	1.2–5.8*	Age, smoking, socioeconomic status
			Jet fuel	OR = 2.5	1.1–5.4	Age, smoking, socioeconomic status
Ref. 13	Occupational histories	Matched for hospital and from population	Petroleum refining and distribution	OR = 4.3†	1.7–10.9*	Age, smoking, weight
Ref. 14	Occupational histories	Other cancer sites	Truck drivers	OR = 3.1†	1.1–8.5	Age, smoking, alcohol
Ref. 15	Interviews	Matched for hospital, sex, and age	Chemical, petrochemical, plastics industries; gasoline and petroleum	OR = 4.0	1.6–9.8	Sex, smoking
Ref. 16	Interviews	General population	Moderate levels of hydrocarbon	OR = 2.7†	1.2–6.5	Weight, education
Ref. 17	Questionnaires	Matched on year of birth, gender, and survival status	Paper and pulp; printing and publishing	OR = 2.20†	1.02–4.72	Obesity, smoking coffee consumption
			Chemicals	OR = 4.19†	1.09–16.1	Obesity, smoking coffee consumption
			Gasoline	OR = 1.72	1.03–2.87	—
Ref. 18	Questionnaires	Matched for expected age	Solvents	OR = 1.54	1.11–2.14	Age, sex, education
			Cutting oils or mists	OR = 1.99	1.23–3.23	Age, sex, education
			Petroleum products	OR = 1.96	1.28–2.99	Age, sex, education
Ref. 19	Interviews	Central Population Register	Gasoline	OR = 2.1†	1.1–4.1	Age, BMI, smoking
			Solvents	OR = 6.4‡	1.8–23	Age, BMI, smoking
			Cutting oils	OR = 2.1†	1.0–4.3	Age, BMI, smoking

Continued.

TABLE 1. Case–control studies of increased risk of kidney cancer and exposure to industrial solvents (*Continued*)

Study	Study design	Control group	Exposure	Result	95% CI	Controlled variables
Ref. 20	Occupational histories	Other cancer sites	Firefighters	OR = 3.51	2.09–5.92	—
			Painters	OR = 1.59	1.00–2.43	—
Ref. 21	Interviews	General population	Dry-cleaning solvents	OR = 1.4†	1.1–1.7	Age, smoking status, BMI, education
			Gasoline	OR = 1.6†	1.2–2.0	Age, smoking status, BMI, education
			Petroleum products	OR = 1.6†	1.3–2.1	Age, smoking status, BMI, education
Ref. 22	Interviews	Matched by region, sex, age	Chemicals (very long duration)	OR = 3.1†	1.2–7.9	Age, smoking
			Organic solvents	OR = 1.6†	1.1–2.3	Age, smoking
			Solvents	OR = 2.1‡	1.0–4.4	Age, smoking
			Paints	OR = 1.3†	1.0–1.6	Age, smoking
			Color films	OR = 2.9†	1.1–8.3	Age, smoking
			Cutting fluids	OR = 1.3†	1.0–1.8	Age, smoking
			Tar, pitch, mineral oil	OR = 2.1‡	1.0–4.5	Age, smoking
				OR = 1.2† (medium exposure);	1.0–1.5 (medium exposure);	
				OR = 1.2† (high exposure);	1.0–1.6 (high exposure);	
				OR = 1.4† (substantial exposure);	1.0–1.9 (substantial exposure);	
				OR = 1.4‡ (medium exposure);	1.0–1.9 (medium exposure);	
				OR = 1.3‡ (high exposure)	1.0–1.8 (high exposure)	

Continued.

TABLE 1. Case–control studies of increased risk of kidney cancer and exposure to industrial solvents (*Continued*)

Study	Study design	Control group	Exposure	Result	95% CI	Controlled variables
			Mineral oil	OR = 1.3†	1.0–1.8	Age, smoking
			Polycyclic aromatic hydrocarbons	OR = 1.3†	1.0–1.6	Age, smoking
Ref. 23	Questionnaires	General population	Benzene	OR = 1.8†	1.3–2.6	Age, education, BMI, smoking, alcohol, meat intake
			Mineral, cutting or lubricating oil	OR = 1.5†	1.2–1.8	Age, education, BMI, smoking, alcohol, meat intake
Ref. 24	Telephone interviews	General population	Automotive dealers and service stations	OR = 2.2†	1.0–4.9	Age, BMI, smoking, meat intake, fruit intake, hypertension, family history
			Automotive repair shops	OR = 4.0†	1.3–12.2	Age, BMI, smoking, meat intake, fruit intake, hypertension, family history
			Mechanics and repairers	OR = 2.0†	1.1–3.5	Age, BMI, smoking, meat intake, fruit intake, hypertension, family history
			Automobile mechanics	OR = 2.9†	1.5–5.8	Age, BMI, smoking, meat intake, fruit intake, hypertension, family history
			Garage and service station	OR = 3.1†	1.0–9.1	Age, BMI, smoking, meat intake, fruit intake, hypertension, family history

† OR reported for males only.
‡ OR reported for females only.
* 90% CI.
CI: confidence interval.

TABLE 2. Cohort studies of increased risk of kidney cancer and exposure to industrial solvents

Study	Study design	Population	Result	95% CI	Controlled variables
Ref. 25	Death certificates	Newspaper pressmen	SMR = 303[†,a]	—	—
Ref. 26	Vital statistics and occupational history	Oil refinery workers, only in maintenance department	SMR = 1,750[†]	293–5781	—
		Oil refinery workers, ever in maintenance department	SMR = 1,112[†]	186–3675	—
Ref. 27	National cancer registries	Service station workers	SIR = 1.3[†]	1.0–1.7	—
Ref. 28	Neste Group workers, Finnish Cancer Registry	Oil and chemicals company workers	SIR = 1.97	1.29–2.88	—
Ref. 29	Swedish Cancer-Environment Registry	Manufacturing industry	SIR = 1.06[†,b]	—	Age, region
Ref. 30	Refinery and chemical plant sites	Baton Rouge workers	SMR = 192	113–303	—

[†]For males only.
[a]$P < 0.05$, [b]$P < 0.01$.
SIR: standardized incidence ratio.
SMR: standardized mortality ratio.

TABLE 3. Summary of patients reported here with occupational exposure to industrial, nonchlorinated solvents

Patient ID	Age (years)	Occupation	Exposure	Duration (years)	Diagnosis (age in years)	Confounding factors
1	60 (deceased)	Automobile mechanic	Industrial solvent	40	Renal cell cancer (35)	Smoked for 2 years; obesity
2	74	Airline mechanic	Industrial solvent	33	Renal cell cancer (67)	Smoked for 35 years; lifetime use of analgesics
3	45	Route serviceman,	Organic solvent	5.5	Renal cell cancer (40)	Smoked for 15 years
4	41	Automobile mechanic	Organic solvent	20	Renal cell cancer (35)	Smoked for 20 years
5	51 (deceased)	Mechanic	Industrial solvent	30	Renal cell cancer (48)	Smoked for 10 years; asbestos; obesity
6	58	Offset stripper	Organic, press and printing solvents	44	Renal cell cancer (50)	Hypertension; overweight
7	65	Machine operator	Industrial, organic solvents and petrochemicals	41	Renal cell cancer (63)	Smoked for 30 years; asbestos; pesticides; chlorinated solvents

duration, diagnosis, and confounding factors. No patient had a family history of renal cancer.

DISCUSSION

Confounding Factors

Six of our patients were smokers. Smoking is a risk factor for kidney cancer, however, regression analysis by the epidemiological study of Hu *et al.* found that the risk of kidney cancer remained elevated after accounting for smoking (OR = 1.8, 95% confidence interval (CI) = 1.3–2.6 for exposure to benzene).[24] Therefore, exposure to industrial solvents containing benzene should be considered as a risk aside from smoking. This finding of smoking and kidney cancer is not surprising because cigarette smoking contributes to the cumulative dose of benzene.[4] Indeed, Hu *et al*. demonstrated the causation role of benzene in kidney cancer. In all likelihood, cigarette smoking is probably an additive factor upon exposure to solvents containing benzene. Three of our patients had increased BMI, a risk factor for kidney cancer. Several epidemiological studies have found significantly increased risk for kidney cancer from exposure to industrial solvents, after regression analysis and controlling for BMI and smoking.[13,17,21,23,24] Therefore, exposure to industrial solvents is considered a distinctive risk factor for kidney cancer, even when accounting for smoking history and BMI.

Although the mechanism is not clear, the common denominator in exposure to industrial solvents is the contents of benzene. Industrial solvents (produced from crude oil) cannot be produced without benzene contamination.[31] Benzene has been shown to be a substantial risk factor for kidney cancer.[23] Because the common denominator in the industrial solvent exposure (nonchlorinated) is also a benzene content, it is reasonable to conclude that benzene, which is a known human carcinogen, is acting as a carcinogenic agent either by itself or in combination with solvent mixture in the causation of kidney cancer.

Benzene in Industrial Solvents

For the last several decades, most organic solvents have been refined from crude oil by a process commonly known as fractional distillation. Benzene is a natural constituent of crude oil. When crude oil is refined to produce refined petroleum distillates, the benzene in the crude oil is not destroyed, but rather ends up as a residual constituent of petroleum distillates. The concentration of benzene in the distillates is largely a function of the quality of the fractional distillation process and other processing methods such as catalytic cracking (which usually increases the benzene content) and hydrotreatment (which usually decreases the benzene content). The highest benzene concentration in

TABLE 4. Duration of exposure to industrial solvents and increased risk of kidney cancer

Study	Exposure	Exposure duration (years)	Result	95% CI
Ref. 16	Moderate levels of hydrocarbon	16–30	OR = 2.4	1.0–6.2
Ref. 19	Hydrocarbons	<20	OR = 2.1†	1.2–3.6
Ref. 26	Petrochemicals	5–15	SMR = 606	101–2002
Ref. 28	Petrochemicals	≥5	SIR = 2.87	1.61–4.73
Ref. 30	Petrochemicals	20–29	SMR = 330*	—

†OR reported for males only.
*Authors report statistical significant results.
SIR: standardized incidence ratio.
SMR: standardized mortality ratio.

solvents has been reported in hexane-based solvents.[32] Following adoption of Occupational Safety and Health Administration's (OSHA) regulation limiting benzene in petroleum hydrocarbon mixtures to no more than 0.1%, the petroleum industry began upgrading fractional distillation and other refining processes.[33] During the 1980s and 1990s, the benzene content of organic solvents decreased rather appreciably, although benzene remains a contaminant of most petroleum solvents today.

Duration of Exposure

Duration of exposure in our cases is described anywhere from 5.5 to 44 years. The scientific literature has addressed the duration of exposure to industrial solvents and the risk of kidney cancer.[16,19,26,28,30] TABLE 4 summarizes these studies, with a range in duration of exposure to industrial solvents from 5 to 30 years. Therefore, the range of exposure described in our patients studied here is within the range described by other studies addressing industrial solvents and increased risk of kidney cancer.

Other Exposures

Patients 5 and 7 have histories of exposure to asbestos. Asbestos exposure has been described as a risk factor for kidney cancer, therefore it is probable that asbestos exposure in patients 5 and 7 also played a substantial role.[21,34–36] Whether the concomitant exposure to asbestos and solvents is additive or synergistic remains unknown for kidney cancer. Patient 7 has been exposed to pesticides. The exposure to pesticides was deemed possible, nevertheless is included in the exposure history. To the best of our knowledge, exposure to pesticides has not been shown to increase risk for kidney cancer. Patient 7 has also been exposed to chlorinated solvents. Some chlorinated solvents have been shown to be a causative risk factor in kidney cancer, therefore it is probable that exposure to chlorinated solvents (if occurred at substantial levels) was also a contributing factor in the causation of kidney cancer in patient 7.[21,37]

CONCLUSION

Based on the reviewed scientific literature and description of our patients, we recommend to occupational physicians for their patients mandatory detailed occupational history, social history, body weight, family history, or other causes, and include exposure to industrial solvents in causation analysis of kidney cancer.

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DISCLOSURE

Some of the comments in this manuscript have been presented in civil court. Nachman Brautbar, M.D. serves from time to time as an expert in litigation related to toxic exposures. He has served as a retained expert in cases of solvent exposure and kidney cancer. This manuscript was not authored for litigation process. Funding for this manuscript was solely provided by Nachman Brautbar, M.D., Inc. The opinions expressed in this manuscript do not necessarily reflect that of any organizations the authors are affiliated with.

REFERENCES

1. Lindblad, P. & H. Adami. 2002. Kidney cancer. *In* Textbook of Cancer Epidemiology. H. Adami, D. Hunter & D. Trichopoulos, Eds.: 467–485. Oxford University Press, Inc. New York, NY.
2. Ferlay, J., F. Bray, P. Pisani, *et al*. 2001. GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide. International Agency for Research on Cancer. Lyon, France.
3. Gnarra, J.R. 1998. Von Hippel-Lindau gene mutations in human and rodent renal tumors—association with clear cell phenotype. J. Natl. Cancer Inst. **90:** 1685–1687.

4. INTERNATIONAL AGENCY FOR RESEARCH ON CANCER. 1986. Tobacco smoking. IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. IARC **38:** 35–394.
5. MCLAUGHLIN, J.K., J.S. MANDEL, W.J. BLOT, *et al*. 1984. A population-based case-control study of renal cell carcinoma. J. Natl. Cancer Inst. **72:** 275–284.
6. MCLAUGHLIN, J.K., P. LINDBLAD, A. MELLEMGAARD, *et al*. International renal-cell cancer study. I. Tobacco use. Int. J. Cancer **60:** 194–198.
7. YUAN, J.M., J.E. CASTELAO, M. GAGO-DOMINGUEZ, *et al*. 1998. Tobacco use in relation to renal cell carcinoma. Cancer Epidemiol. Biomarkers Prev. **7:** 429–433.
8. WOLK, A., P. LINDBLAD & H.O. ADAMI. 1996. Nutrition and renal cell cancer. Cancer Causes Control **7:** 5–18.
9. BENICHOU, J., W.H. CHOW, J.K. MCLAUGHLIN, *et al*. 1998. Population attributable risk of renal cell cancer in Minnesota. Am. J. Epidemiol. **148:** 424–430.
10. LINDBLAD, P., W.H. CHOW, J. CHAN, *et al*. The role of diabetes mellitus in the aetiology of renal cell cancer. Diabetologia **42:** 107–112.
11. GOTTLIEB, M.S. & J.K. CARR. 1981. Mortality studies on lung, pancreas, esophageal, and other cancers in Louisiana. *In* Banbury Report 9: Quantification of Occupational Cancer. R. Peto & M. Schneiderman, Eds.: 195–204. Cold Spring Harbor Laboratory. Cold Spring Harbor, NY.
12. SIEMIATYCKI, J., R. DEWAR, L. NADON, *et al*. 1987. Associations between several sites of cancer and twelve petroleum-derived liquids. Results from a case-referent study in Montreal. Scand. J. Work Environ. Health **13:** 493–504.
13. ASAL, N.R., J.R. GEYER, D.R. RISSER, *et al*. 1988. Risk factors in renal cell carcinoma. II. Medical history, occupation, multivariate analysis, and conclusions. Cancer Detect. Prev. **13:** 263–279.
14. BROWNSON, R.C. 1988. A case-control study of renal cell carcinoma in relation to occupation, smoking, and alcohol consumption. Arch. Environ. Health **43:** 238–241.
15. JENSEN, O.M., J.B. KNUDSEN, J.K. MCLAUGHLIN, *et al*. 1988. The Copenhagen case-control study of renal pelvis and ureter cancer: role of smoking and occupational exposures. Int. J. Cancer **41:** 557–561.
16. KADAMANI, S., N.R. ASAL & R.Y. NELSON. 1989. Occupational hydrocarbon exposure and risk of renal cell carcinoma. Am. J. Ind. Med. **15:** 131–141.
17. PARTANEN, T., P. HEIKKILA & S. HERNBERG, *et al*. 1991. Renal cell cancer and occupational exposure to chemical agents. Scand. J. Work Environ. Health. **17:** 231–239.
18. MCCREDIE, M. & J.H. STEWART. 1993. Risk factors for kidney cancer in New South Wales. IV. Occupation. Br. J. Ind. Med. **50:** 349–354.
19. MELLEMGAARD, A., G. ENGHOLM, J.K. MCLAUGHLIN, *et al*. 1994. Occupational risk factors for renal-cell carcinoma in Denmark. Scand. J. Work Environ. Health **20:** 160–165.
20. DELAHUNT, B., P.B. BETHWAITE & J.N. NACEY. 1995. Occupational risk for renal cell carcinoma. A case-control study based on the New Zealand Cancer Registry. Br. J. Urol. **75:** 578–582.
21. MANDEL, J.S., J.K. MCLAUGHLIN, B. SCHLEHOFER, *et al*. 1995. International renal-cell cancer study. IV. Occupation. Int. J. Cancer. **61:** 601–605.
22. PESCH, B., J. HAERTING, U. RANFT, A. KLIMPEL, *et al*. 2000. Occupational risk factors for renal cell carcinoma: agent-specific results from a case-control study

in Germany. MURC Study Group. Multicenter urothelial and renal cancer study. Int. J. Epidemiol. **29:** 1014–1024.
23. HU, J., Y. MAO & K. WHITE. 2002. Renal cell carcinoma and occupational exposure to chemicals in Canada. Occup. Med. (Lond.) **52:** 157–164.
24. ZHANG, Y., K.P. CANTOR, C.F. LYNCH, *et al*. 2004. A population-based case-control study of occupation and renal cell carcinoma risk in Iowa. J. Occup. Environ. Med. **46:** 235–240.
25. PAGANINI-HILL, A., E. GLAZER, B.E. HENDERSON, *et al*. 1980. Cause-specific mortality among newspaper web pressmen. J. Occup. Med. **22:** 542–544.
26. BERTAZZI, P.A., A.C. PESATORI, C. ZOCCHETTI, *et al*. 1989. Mortality study of cancer risk among oil refinery workers. Int. Arch. Occup. Environ. Health. **61:** 261–270.
27. LYNGE, E., A. ANDERSEN, R. NILSSON, *et al*. 1997. Risk of cancer and exposure to gasoline vapors. Am. J. Epidemiol. **145:** 449–458.
28. PUKKALA, E. Cancer incidence among Finnish oil refinery workers, 1971–1994. J. Occup. Environ. Med. **40:** 675–679.
29. MCLAUGHLIN, J.K., H.S. MALKER, B.J. STONE, *et al*. 1987. Occupational risks for renal cancer in Sweden. Br. J. Ind. Med. **44:** 119–123.
30. SHALLENBERGER, L.G., J.F. ACQUAVELLA & D. DONALESKI. 1992. An updated mortality study of workers in three major United States refineries and chemical plants. Br. J. Ind. Med. **49:** 345–354.
31. MEHLMAN, M.A. 2004. Benzene: a haematopoietic and multi-organ carcinogen at any level above zero. Eur. J. Oncol. **9:** 15–36.
32. SHELL OIL COMPANY. 1977. Benzene content of Shell hydrocarbon solvents. Houston, TX. July.
33. OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION. 1978. Benzene. Final rules. Standard number: 1910.1028. Federal Register. **43:** 27962–27971.
34. SELIKOFF, I.J., E.C. HAMMOND & H. SEIDMAN. 1979. Mortality experience of insulation workers in the United States and Canada. Ann. N. Y. Acad. Sci. **330:** 91–116.
35. ENTERLINE, P.E., J. HARTLEY & V. HENDERSON. 1987. Asbestos and cancer: a cohort followed up to death. Br. J. Ind. Med. **44:** 396–401.
36. MACLURE, M. 1987. Asbestos and renal adenocarcinoma: a case-control study. Environ. Res. **42:** 353–361.
37. BRUNING, T., B. PESCH, B. WIESENHUTTER, *et al*. 2003. Renal cell cancer risk and occupational exposure to trichloroethylene: results of a consecutive case-control study in Arnsberg, Germany. Am. J. Ind. Med. **43:** 274–285.