Parental Occupational Exposures and Risk of Childhood Cancer

Joanne S. Colt and Aaron Blair

Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, Maryland

Occupational exposures of parents might be related to cancer in their offspring. Forty-eight published studies on this topic have reported relative risks for over 1000 specific occupation/cancer combinations. Virtually all of the studies employed the case–control design. Occupations and exposures of fathers were investigated much more frequently than those of the mother. Information about parental occupations was derived through interviews or from birth certificates and other administrative records. Specific exposures were typically estimated by industrial hygienists or were self-reported. The studies have several limitations related to the quality of the exposure assessment, small numbers of exposed cases, multiple comparisons, and possible bias toward the reporting of positive results. Despite these limitations, they provide evidence that certain parental exposures may be harmful to children and deserve further study. The strongest evidence is for childhood leukemia and paternal exposure to solvents, paints, and employment in motor vehicle-related occupations; and childhood nervous system cancers and paternal exposure to paints. To more clearly evaluate the importance of these and other exposures in future investigations, we need improvements in four areas: *a*) more careful attention must be paid to maternal exposures; *b*) studies should employ more sophisticated exposure assessment techniques; *c*) careful attention must be paid to the postulated mechanism, timing, and route of exposure; and *d*) if postnatal exposures are evaluated, studies should provide evidence that the exposure is actually transferred from the workplace to the child's environment. — *Environ Health Perspect* 106(Suppl 3):909–925 (1998). *http://ehpnet1.niehs.nih.gov/docs/1998/Suppl-3/909-925colt/abstract.html*

Key words: children, cancer, occupation, occupational exposure, leukemia, lymphoma, brain tumor, neuroblastoma, Wilms tumor

Introduction

The incidence of childhood cancer has been increasing nearly one percent per year for the past two decades (*1*). This increase is largely unexplained, but exposure to environmental chemicals is a concern. Because the workplace is an important source of environmental chemicals and these chemicals may be inadvertently transferred from the workplace to the home, special attention has been paid to the relationship between parental occupation and the risk of childhood cancer.

Savitz and Chen (*2*) reviewed the literature on this topic in 1990. Their review covered 24 papers and focused on the methodologies used, the findings for specific occupation/cancer combinations, and the need for further study. The body of literature has grown considerably since then, with twice as many studies published to date. This review takes another look at the relationship between cancer in children and the occupations of their parents.

Methods

Forty-eight published epidemiologic studies were reviewed for this paper, 22 of which were published subsequent to Savitz and Chen's review. These studies provided relative risks for over 1000 specific cancer/occupation or cancer/exposure combinations. To sort through this welter of data, our first step was to create a database tracking each relative risk and the occupation, industry, or exposure to which it applied, according to the author. We then combined occupations and exposures into categories to facilitate the analysis. For example, we created a category called paints and pigments and included findings that authors reported for paints and pigments, painting and printing occupations, and the newspaper and printing industry. The reader is cautioned that occupations grouped together because of a common exposure may have overlapping exposures to other potentially carcinogenic agents.

We then developed a set of criteria to identify the most promising leads for evaluation and further work. We focus only on *a*) findings that pertained to a specific childhood cancer as opposed to all cancers combined, *b*) cancer/occupation/exposure categories with significantly elevated relative risks in two or more studies, and *c*) relative risks based on two or more exposed cases. For cancer/occupation/exposure categories that meet these criteria, we present all the relative risks reported, regardless of whether they are excesses or deficits. Along with each relative risk, we also present the number of exposed cases to provide an indication of the power of the study to detect a significant association.

Because we are interested primarily in potentially hazardous occupational exposures, we have chosen not to report results for occupations in which hazardous exposures are unlikely, such as professionals, sales workers, and clerical workers. Savitz and Chen pointed out that some studies have shown elevated childhood cancer risks for these occupations and attributed this to effects of high social class rather than to chemical exposures. We have excluded findings related to pesticides because these chemicals are evaluated in another paper in these proceedings (*3*). Finally, we do not report results for broadly defined occupational groupings (e.g., manufacturing, service occupations), as they lack the necessary precision to identify specific exposures deserving future attention.

Results

Overview of the Studies

Virtually all of the studies employed the case–control design. Exceptions were a proportionate mortality study by Sanders et al. (*4*) and an investigation of a possible cancer cluster by Wilkins et al. (*5*). The majority of the studies (about 80%) were incidence-based (Table 1). Although most

---

This paper is based on a presentation at the U.S. EPA Conference on Preventable Causes of Cancer in Children held 15–16 September 1997 in Arlington, Virginia. Manuscript received at *EHP* 4 December 1997; accepted 24 March 1998.

Address correspondence to J.S. Colt, National Cancer Institute, 6130 Executive Boulevard, Room 418, Rockville, MD 20892. Telephone: (301) 435-4704. Fax: (301) 402-1819. E-mail: coltj@epndce.nci.nih.gov

Abbreviations used: ALL, acute lymphocytic leukemia; ANLL, acute nonlymphocytic leukemia; CI, confidence interval; CNS, central nervous system; EMF, electromagnetic fields; HCs, hydrocarbons; IH, industrial hygienist; JEM, job exposure matrix; NHL, non-Hodgkin's lymphoma; OR, odds ratio.

Table 1. Overview of 48 studies of childhood cancer and parental occupations.

Reference	Exposure assessment methodology	Time frame of exposure	Upper age limit	Incidence or mortality	Person exposed	Childhood malignancies covered
Included in Savitz and Chen (1990) (*2*) review						
Fabia and Thuy, 1974 (*17*)	Birth certificates + IH assessment	At birth	4	Mortality	Father	Total cancer, leukemia + lymphoma, nervous system, Wilms
Kantor et al., 1979 (*46*)	Birth certificate + Fabia and Thuy (*17*) classification	At birth	19	Incidence	Father	Wilms
Kwa and Fine, 1980 (*20*)	Birth certificate + Fabia and Thuy (*17*) classification	At birth	14	Mortality	Father	Total cancer, leukemia + lymphoma, nervous system, urinary system
Zack et al., 1980 (*41*)	Questionnaire + IH assessment	Year before birth, at birth, after birth	15	Incidence	Father	Total cancer, leukemia + lymphoma, nervous system, Wilms
Peters et al., 1981 (*11*)	Questionnaire with self-reported exposures	Preconception through postnatal	9	Incidence	Father, mother	Brain
Hemminki et al., 1981 (*12*)	Occupations collected from maternal welfare centers	During pregnancy	14	Incidence	Father, mother	Total cancer, leukemia, brain
Sanders et al., 1981 (*4*)	Child's death certificate + IH assessment	At child's death	14	Mortality	Father	Total cancer, leukemia, brain, kidney
Gold et al., 1982 (*18*)	Questionnaire + IH assessment	Before birth, after birth	19	Incidence	Father, mother	Leukemia, brain
Prestin-Martin et al., 1982 (*26*)	Questionnaire	During pregnancy	24	Incidence	Mother	Brain
Wilkins and Sinks, 1984 (*47*)	Birth certificate + Zack (*41*) classification	At birth	NA	Incidence	Father	Wilms
Wilkins and Sinks, 1984 (*48*)	Birth certificate + JEM	At birth	NA	Incidence	Father	Wilms
Hicks et al., 1984 (*34*)	Questionnaire + IH assessment	Year before birth	15	Incidence	Father, mother	Total cancer, leukemia + lymphoma, nervous system, Wilms, bone, rhabdomyosarcoma, retinoblastoma
Vianna et al., 1984 (*33*)	Questionnaire + IH assessment	Before birth	1	Incidence	Father	Acute leukemia
Shaw et al., 1984 (*54*)	Birth certificate + IH assessment	At birth	15	Incidence	Father	Leukemia
Van Steensel-Moll et al., 1985 (*31*)	Questionnaire with self-reported exposures + Zack (*41*) classification	During pregnancy, after birth	14	Incidence	Father, mother	ALL
Spitz and Johnson, 1985 (*6*)	Birth certificate + clustering scheme	At birth	14	Mortality	Father	Neuroblastoma
Olshan et al., 1986 (*55*)	Questionnaire	Before birth, after birth	15	Incidence	Father	Brain
Lowengart et al., 1987 (*28*)	Questionnaire with self-reported exposure + IH assessment	Preconception, during pregnancy, after birth	10	Incidence	Father	Acute leukemia
Johnson et al., 1987 (*13*)	Birth certificate + HC-related jobs according to past studies	At birth	14	Mortality	Father	Intracranial and spinal cord
Wilkins and Koutras, 1988 (*7*)	Birth certificate	At birth	19	Mortality	Father	Brain
Nasca et al., 1988 (*21*)	Questionnaire + Zack (*41*), Hicks (*34*), Spitz (*6*) classifications	At birth, at diagnosis	14	Incidence	Father, mother	Nervous system
Shu et al., 1988 (*43*)	Questionnaire with self-reported exposures	Preconception, during pregnancy	15	Incidence	Father, mother	Leukemia
Buckley et al., 1989 (*27*)	Questionnaire with self-reported exposures + JEM	Lifetime	18	Incidence	Father, mother	ANLL
Bunin et al., 1989 (*44*)	Questionnaire + JEM + clustering scheme	Preconception, during pregnancy, after birth	14	Incidence	Father, mother	Wilms

(*Continued*)

Table 1. *Continued.*

Reference	Exposure assessment methodology	Time frame of exposure	Upper age limit	Incidence or mortality	Person exposed	Childhood malignancies covered
Not included in Savitz and Chen (1990) (*2*) review						
Hakulinen et al., 1976 (*19*)	Occupation reported to maternity welfare district + Fabia and Thuy (*17*) classification	During pregnancy	14	Incidence	Father	Total cancer, leukemia + lymphoma, brain
Gold et al., 1979 (*56*)	Questionnaire with self-reported exposures	Before birth, after birth	19	Incidence	Father, mother	Brain
Howe et al., 1989 (*24*)	Questionnaire	Before birth	19	Incidence	Father, mother	Brain
Johnson and Spitz, 1989 (*8*)	Birth certificate + Spitz (*6*) classification	At birth	14	Mortality	Father	Nervous system
Wilkins and Sinks, 1990 (*16*)	Questionnaire + JEM + clustering scheme	Preconception, during pregnancy, after birth	19	Incidence	Father, mother	Brain
Bunin et al., 1990 (*57*)	Questionnaire + Spitz (*6*) classification	Preconception, during pregnancy	NA	Incidence	Father, mother	Neuroblastoma
Bunin et al., 1990 (*58*)	Questionnaire + JEM + clustering scheme	Preconception, postconception	NA	Incidence	Father, mother	Retinoblastoma
Wilkins and Hundley, 1990 (*25*)	Questionnaire + JEM + clustering scheme	At birth	15	Incidence	Father	Neuroblastoma
Gardner et al., 1990 (*35*)	Birth certificate, questionnaire + industry dosimetry records	Preconception, at birth	24	Incidence	Father	Leukemia, leukemia + NHL
Magnani et al., 1990 (*32*)	Questionnaire	Before birth, after birth	NA	Incidence	Father, mother	ALL, ANLL, NHL
Olsen et al., 1991 (*23*)	Pension fund files	At time of conception, most recent	20	Incidence	Father, mother	Total cancer, leukemia + lymphoma, central nervous system, sympathetic nervous system, renal, bone, retinoblastoma, hepatic, sarcoma, germ cell
Infante-Rivard et al., 1991 (*42*)	Questionnaire with self-reported exposures + IH assessment	During pregnancy	14	Incidence	Mother	ALL
Wilkins et al., 1991 (*5*)	Questionnaire	Preconception,during pregnancy, after birth	19	Incidence	Father, mother	Intracranial tumors
McKinney et al., 1991 (*29*)	Questionnaire with self-reported exposures	Preconception, during pregnancy, after birth	14	Incidence	Father, mother	Leukemia + NHL
Urquhart et al., 1991 (*37*)	Questionnaire + occupational records on radiation dose	Preconception	14	Incidence	Father	Leukemia + NHL
Kuijten et al., 1992 (*9*)	Questionnaire + Hicks (*34*) and Vianna (*33*) classifications	Preconception, during pregnancy, after birth	14	Incidence	Father, mother	Brain (astrocytoma)
Feingold et al., 1992 (*22*)	Questionnaire + JEM	Year prior to birth	14	Incidence	Father, mother	Total cancer, ALL, brain
Sorahan et al., 1993 (*40*)	Questionnaire + IH assessment	Preconception	15	Mortality	Father	Total cancer, leukemia, leukemia + lymphoma
McLaughlin et al., 1993 (*39*)	Linkage with National Dose Registry	Preconception	14	Incidence	Father	Leukemia
Roman et al., 1993 (*36*)	Questionnaire + linkage to nuclear industry database	Preconception, during pregnancy, after birth	4	Incidence	Father, mother	Leukemia + NHL
Kinlen et al., 1993 (*38*)	Scottish nuclear industry and National Radiological Protection Board	Preconception	24	Incidence	Father	Leukemia, leukemia + NHL
Sorahan et al., 1995 (*59*)	Questionnaire + IH assessment	Preconception, postconception	15	Mortality	Father	Total cancer
Wilkins and Wellage, 1996 (*60*)	Questionnaire + classification scheme	Preconception, during pregnancy	19	Incidence	Father	Nervous system
Gelberg et al., 1997 (*61*)	Questionnaire	During pregnancy, after birth	24	Incidence	Father, mother	Osteosarcoma

Abbreviations: IH, industrial hygienist; JEM, job exposure matrix; NA, not available from published report; NHL, Non-Hodgkin lymphoma.

studies limited the maximum age of cases to the teen years, four were restricted to children under 10 years of age and five investigations included young adults 20 years of age or older (the maximum age is 24 years). The number of investigations varied by tumor. Cancers of the nervous system (26 studies) and leukemia/lymphomas (25 studies) have received the most attention. Ten studies examined urinary system cancers, only one of which was published after Savitz and Chen's review, and bone cancer and retinoblastoma were each addressed in three studies.

Occupations and exposures of fathers have been investigated much more frequently than those of the mother. Forty-six of the 48 studies examined paternal occupations or exposures, but only about half of the studies addressed maternal occupations or exposures. This is somewhat surprising as maternal exposures are clearly more important for fetal exposure than paternal. Maternal occupations have received somewhat more attention in the more recent studies.

Several methods were used to obtain occupational information, and the way this information was used in analyses varied. Thirty-one studies obtained information about parents' occupations from questionnaires administered to one or both parents, 11 used the parental occupation listed on the child's birth certificate, and 6 studies used other records such as the child's death certificate, maternal health records, or pension fund files. About one-fifth of the studies presented cancer risks only for job titles, whereas the majority of the studies calculated odds ratios for specific exposures as well as job titles. In studies evaluating specific chemicals, exposures were typically based on estimates by industrial hygienists (IH) or from established job exposure matrices. In 7 studies, occupational exposures were self-reported.

Although the timing of exposure is relevant to the mechanism of action, it was not always clearly indicated in the reports. Risk of childhood cancer could occur from damage to germ cells (for exposures that occur prior to conception) or from direct effects on the individual (transplacental or postnatal exposure). Some studies reported results for two or more time periods (e.g., before and after conception, before and after birth), and a few reported results for three periods (preconception, during pregnancy, and after birth). Overall, the preconception, pregnancy, and postnatal periods have received about equal attention in the literature, with the preconception period receiving increased attention in the more recent studies.

Nervous System Cancers

Of the 26 studies that looked at nervous system cancers, over half focused on brain tumors. Three studies focused exclusively on neuroblastoma, a malignancy whose etiology could be different from those of the other nervous system cancers. Paternal exposures with significant associations with childhood nervous system cancers in multiple studies include electromagnetic fields (EMF), paints and pigments, hydrocarbons (HCs), metals, and paternal employment in motor vehicle-related occupations (Table 2). The first three of these categories were also identified by Savitz and Chen as exposures that warrant further study.

In 1985, Spitz and Johnson (*6*) reported a significant increase in neuroblastoma deaths among children whose fathers had worked in a group of occupations classified as having EMF exposure. Several significant associations between various cancers of the nervous system and individual occupations believed to involve EMF exposure have been reported since then, including work in electrical assembly/installation/repair occupations (*7*); electricians, construction electricians, and workers in electronics manufacturing industries (*8*); employment at a electronic components manufacturing plant (*5*); and electrical repair workers (*9*). A number of other nonsignificant associations with possible EMF-related jobs have been reported. Brain cancer among adults has been associated with employment in electricity-related occupations in a number of studies (*10*).

Paternal exposure to paints and/or inks has been implicated as a risk factor for childhood cancers of the nervous system in most investigations that have evaluated this issue (*9,11–13*). Many relative risks were statistically significant and several were quite large (i.e., 5.0 or larger). Brain cancer in adults has been associated with solvent-related occupations (*14*), and many solvents have nonneoplastic neurobehavioral effects (*15*). It is interesting to note that in the study by Wilkins and Sinks (*16*), brain cancer risk was elevated among children of fathers occupationally exposed to certain aromatic amines that have been used in some dyes and pigments.

In the earliest study of parental occupation and childhood cancer, Fabia and Thuy (*17*) noted a significant 3-fold increase in deaths from nervous system cancers from parental occupational contact with HCs. Many others have presented results on this exposure, with significant excesses observed in two studies (*6,18*). However, the finding by Gold et al. (*18*) was not consistent for different control groups and the authors concluded that the study did not support such an association. For six other studies (*4,13,19–22*), the relative risks for nervous system cancer and parental occupations with potential hydrocarbon exposure were unimpressive. Many of the relative risks were less than 1.0, and those that exceeded 1.0 did so only slightly and the differences were not significant. Exposures in this grouping of occupations are quite varied in terms of the specific chemicals and levels involved; thus an inconsistent pattern of risk is not surprising.

Paternal occupations and industries associated with metals were found to be significantly associated with brain cancer in two studies (*7,16*), but studies by Kuijten et al. (*9*) and Feingold et al. (*22*) showed little evidence for such an association. Metals generally have not been associated with the development of brain cancers in adults or in experimental animals (*10*).

Paternal employment in motor vehicle-related occupations was significantly associated with childhood nervous system cancers in two studies (*17,23*), and two other studies had elevated relative risks but small numbers of exposed cases (*16,24*). However, most studies that have examined these types of occupations have not found an association (*7,9,12,13,18–20,25*), with relative risks typically less than 1.0. Adult brain cancer generally has not been found to be excessive among various motor vehicle drivers (*10*).

Four other paternal occupations/exposures were named as promising leads for further study of childhood nervous system cancers by Savitz and Chen: the pulp and paper industry, the chemical industry, the petroleum industry, and ionizing radiation. The pulp and paper industry was examined in three studies subsequent to Savitz and Chen's review, with odds ratios (ORs) ranging from 0.8 to 5.0, none of them statistically significant; the prevalence of exposure was low (*9,16,25*). Two recent studies of the chemical industry found elevated ORs (*9,23*), one of them significant (*23*). No association was found in a study that combined chemical and petroleum refinery workers (*9*). Only one study of ionizing radiation has been performed since 1990 (*9*), and no association was found.

Table 2. Childhood nervous system cancers and paternal occupations with significant findings in multiple studies.

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
Electromagnetic fields								
Spitz and Johnson, 1985 (*6*)	Neuro-blastoma	Electricians, electric and electronic workers, linemen, welders, utility employees	EMF	At birth	2.14	0.95–4.8	13	
		Electricians, electric and electronic workers, linemen, welders, utility employees, electrical equipment salesmen and repairmen	EMF		2.13	1.05–4.4	17	
		Electronics workers only	EMF		11.75	1.4–98.6	6	
Wilkins and Koutras, 1988 (*7*)	Brain	Structural work: electrical assembling, installation, and repair occupations		At birth	2.70	1.2–6.1	19	
		Machinery industry: electrical assembly, installation, repair occupations			3.60	1.3–10.0	16	
		Bench occupations: assembly and repair of electrical equipment			1.00	0.3–3.7	4	
Nasca et al., 1988 (*21*)	Nervous system	Electricians, electronics workers, power linemen	EMF	At birth	1.70	0.8–3.6	15	
				At diagnosis	1.28	0.6–2.9	11	
		Electricians, electronics workers, power linemen, electric equipment repairmen, utility workers	EMF	At birth	1.61	0.8–3.1	19	
				At diagnosis	1.14	0.5–2.5	12	
Johnson and Spitz, 1989 (*8*)	Central nervous system	Industries	EMF	At birth	1.64	0.96–2.8	25	
		Electronics manufacturing	EMF		3.56	1.04–12.2	7	
		Computer and office machine manufacturing	EMF		4.07	0.7–22.3	4	
		Refrigeration and air conditioning manufacturing	EMF		1.36	0.2–8.2	2	
		Electrical and electronic apparatus manufacturing	EMF		1.42	0.5–3.8	7	
		Elecronic components manufacturing	EMF		3.05	0.5–18.3	3	
		Telephone communications	EMF		1.22	0.3–5.1	3	
		Electric utilities	EMF		2.71	0.6–12.2	4	
		Electric repair	EMF		1.63	0.4–6.1	4	
		Occupations	EMF		1.44	0.9–2.4	28	
		Radio operators	EMF		2.01	0.3–14.3	2	
		Electrical goods and applicance salesmen	EMF		1.01	0.2–5.5	2	
		Computer and business machine, power plant, utilities service mechanics	EMF		2.68	0.6–12.0	4	
		Electrical and electronics assemblers and mechanics	EMF		2.01	0.5–8.1	4	
		Electronics assemblers and mechanics	EMF		3.01	0.5–18.1	3	
		Electrical and electronics assemblers, installers, mechanics	EMF		1.34	0.6–3.0	10	
		Electricians	EMF		3.52	1.02–12.1	7	
		Construction electricians	EMF		10.05	1.2–86.3	5	
Bunin et al., 1990 (*57*)	Neuro-blastoma	Electricians; electrical and electronics workers; linemen, welders, utility employees	EMF	Preconception	1.30	0.4–4.1	16[a]	
				During pregnancy	0.30	0.1–1.3	12[a]	
		Electricians; electrical and electronics workers; linemen, welders, utility employees; electrical equipment salesmen and repairmen	EMF	Preconception	1.00	0.4–2.3	28[a]	
				During pregnancy	0.60	0.2–1.6	19[a]	
		Electrical and electronic products workers	EMF	Preconception	1.60	0.5–6.2	13[a]	
				During pregnancy	0.40	0.1–1.6	11[a]	
		Electrical and electronic products assemblers	EMF	Preconception	4.00	0.4–195	5[a]	

(*Continued on next page*)

Table 2. *Continued.*

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
Wilkins and Hundley, 1990 (*25*)	Neuro-blastoma	Different clustering schemes	EMF	At birth	0.5–1.9	NS	4–24	
Wilkins et al., 1991 (*5*)	Brain	Electronic components manufacturer			73.30	26.5–157.5	6	Standardized incidence ratio for possible cancer cluster
Kuijten et al., 1992 (*9*)	Brain (astrocytoma)	Electrical assembling, installing, repair		Preconception	1.00	0.4–2.8	18[a]	
				During pregnancy	1.00	0.3–3.7	12[a]	
				After birth	1.00	0.3–3.7	12[a]	
		Electrical repair only		Preconception	8.00	1.1–356	9[a]	
				During pregnancy	5.00	0.6–237	6[a]	
				After birth	2.50	0.4–26.2	7[a]	
			EMF (definite)	Preconception	1.10	0.4–3.1	19[a]	
				During pregnancy	0.90	0.3–2.6	17[a]	
				After birth	0.80	0.2–2.3	16[a]	
			EMF (probable)	Preconception	1.70	0.7–4.4	27[a]	
				During pregnancy	1.60	0.6–4.5	21[a]	
				After birth	1.30	0.5–3.6	21[a]	
Wilkins and Wellage, 1996 (*60*)	Brain		EMF	Preconception	1.31	0.6–3.0	11	
				During pregnancy	1.03	0.5–2.4	9	
		Welding-related employment	EMF	Preconception	3.83	0.95–15.6	6	
				During pregnancy	2.50	0.7–9.3	5	
		Welding	EMF	Preconception	1.75	0.2–13.2	3	
				During pregnancy	1.00	0.1–11.0	2	
Paints and pigments								
Kwa and Fine, 1980 (*20*)	Nervous system	Printers		At birth	NA	NS	2	
Peters et al., 1981 (*11*)	Brain		Paints	Year before pregnancy through diagnosis	7.00	S	7	
Hemminki et al., 1981 (*12*)	Brain	Painter		During pregnancy	2.59	NS	14[a]	Results for entire study period
					5.00	S		
							7[a]	Results for 1969–1975 only
Johnson et al., 1987 (*13*)	Nervous system	Painters	HCs	At birth	1.00	0.3–3.3		
		Printing workers	HCs		4.50	1.4–14.7	9	
		Graphic arts workers	HCs		21.90	1.2–397	5	
		Newspaper and printing industries	HCs		5.10	1.6–16.3	10	
Kuijten et al., 1992 (*9*)	Brain (astrocytoma)	Newspaper and printing industry		Preconception	1.50	0.4–7.2	10[a]	
				During pregnancy	1.30	0.7–6.3	9[a]	
				After birth	1.20	0.3–4.2	13[a]	
		Printing workers		Preconception	4.00	0.4–195	5[a]	
				During pregnancy	3.00	0.2–157	4[a]	
				After birth	2.50	0.4–26.2	7[a]	
			Paint	After birth	Infinity	0.7–infinity	4[a]	
Hydrocarbons								
Fabia and Thuy, 1974 (*17*)	Nervous system	Motor vehicle mechanic, service station attendant	HCs	At birth	[2.82]	S	10	
		Machinist, miner, lumberman	HCs		[0.42]	NS	2	
Hakulinen et al., 1976 (*19*)	Brain	Motor vehicle drivers	HCs	During pregnancy	0.67	0.3–1.5	[16]	
		Motor vehicle mechanics, machinists, miners, painters, dyers, printers	HCs		1.40	0.5–3.9	[11]	
		Motor vehicle mechanics, machinists, miners, painter, dyers, printers, motor vehicle drivers	HCs		0.88	0.5–1.7	[27]	

(*Continued*)

Table 2. *Continued.*

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative Risk	95% CI	Number of exposed cases	Comments
Kwa and Fine, 1980 (*20*)	Nervous system	Mechanics, service station attendants	HCs	At birth	1.00	NS	6	ORs were calculated by Savitz and Chen (1990) (*2*)
		Machinists	HCs		0.70	NS	9	
Sanders at al., 1981 (*4*)	Brain	Miners, engineering and allied trades, textiles, printing press operators, painters and decorators, dry cleaners, motor vehicle drivers	HCs	At child's death	0.91	NS	260	
Gold et al., 1982 (*18*)	Brain	Factory workers, machinists, drivers, motor vehicle mechanics, service station	HCs	Before birth	0.54–2.3	NS	10–20[a]	Results are for two control groups
		attendants, lumbermen,	HCs	After birth	0.85	NS	24[a]	Healthy controls
		painters, dyers, cleaners	HCs		4.00	S	15[a]	Cancer controls
Spitz and Johnson, 1985 (*6*)	Neuro-blastoma		HCs	At birth	NA	NS	NA	
			Aromatic and aliphatic HCs		3.17	1.1–8.9	10	
Johnson et al., 1987 (*13*)	Nervous system		HCs	At birth	0.7–1.1	NS	NA	Results are for different groups of HC-related jobs
		Aircraft industry workers	HCs		1.00	0.5–2.3	NA	
		Machine repairmen	HCs		1.50	0.8–2.7	NA	
		Paper and pulp mill workers	HCs		4.00	0.4–43.7	NA	
		Factory workers, machinists, steelworkers	HCs		1.20	0.9–1.6	NA	
		Motor vehicle mechanics, machinists, miners, painters, dyers, printers	HCs		1.00	0.7–1.6	NA	
		Motor vehicle mechanics, service station attendants	HCs		0.70	0.3–1.5	NA	
Nasca et al., 1988 (*21*)	CNS	Narrow definition	HCs	At birth	1.25	0.7–2.4	18	
				At diagnosis	1.11	0.5 –2.3	13	
		Broad definition	HCs	At birth	1.41	0.9–2.2	38	
				At diagnosis	1.22	0.7–2.0	29	
Feingold et al., 1992 (*22*)	Brain		HCs	During pregnancy	0.80	0.3–2.0	18	
			Aromatic HCs		1.10	0.4–3.0	18	
			Alicyclic HCs		0.80	0.2–4.4	4	
			Alkylating agents		1.30	0.4-4.0	9	
			Aliphatic HCs		0.80	0.3–2.2	15	
Metals								
Wilkins and Koutras, 1988 (*7*)	Brain	Metal industry		At birth	1.80	1.1–2.9	62	
		Metal related occupations			1.60	1.1–2.3	93	
		Metal industry: processing occupations			5.30	1.0–27.2	9	
		Metal industry: machine trades occupations			1.40	0.6–3.2	17	
		Metal industry: structural work occupations			3.90	1.2–12.8	12	
		Machine trades occupations: metal machining occupations			1. 10	0.6–1.8	30	

(*Continued on next page*)

Table 2. *Continued.*

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
Wilkins and Koutras, 1988 (*7*)	Brain	Machine trades occupations: metalworking occupations			1.60	0.7–3.7	14	
		Processing occupations: occupations in processing of metal			5.00	0.6–46.1	4	
		Bench occupations: fabrication, assembly, repair of metal products			1.40	0.6–3.4	12	
		Structural work: occupations in metal fabricating			2.60	0.8–8.7	10	
Wilkins and Sinks, 1990 (*16*)	Brain	Metal industry		Preconception	3.30	1.3–8.5	13	
				During pregnancy	2.00	0.8–5.1	10	
				After birth	1.70	0.7–3.7	16	
Kuijten et al., 1992 (*9*)	Brain (astrocytoma)	Metal-related occupations		Preconception	1.10	0.5–2.1	41[a]	
				During pregnancy	0.90	0.4–2.0	32[a]	
				After birth	0.80	0.4–1.8	33[a]	
Feingold et al., 1992 (*22*)	Brain		Inorganics (metals and metalloids)	During pregnancy	1.20	0.4–3.3	17	Odds ratios for individual metals were not significant
Motor vehicle-related occupations								
Fabia and Thuy, 1974 (*17*)	Nervous system	Motor vehicle mechanic, service station attendant	HCs	At birth	[2.82]	S	10	
Hakulinen et al., 1976 (*19*)	Brain	Motor vehicle drivers	HCs	During pregnancy	0.67	0.3–1.5	[16]	
Kwa and Fine, 1980 (*20*)	Nervous system	Motor vehicle driver		After birth	0.60	NS	5	ORs calculated by Savitz and Chen (1990) (*2*)
		Mechanics, gas station attendants	HCs	At birth	1.00	NS	6	
Hemminki et al., 1981 (*12*)	Brain	Motor vehicle driver		During pregnancy	0.92	NS	84[a]	
Gold et al., 1982 (*18*)	Brain	Driver, mechanic, service station attendant, railroad worker/engineer		Before birth	0.33–0.50	NS	6–12[a]	Results are for two control groups
		Driver		After birth	0.67–1.00	NS	10–15[a]	
Johnson et al., 1987 (*13*)	Nervous system	Motor vehicle mechanics, service station attendants	HCs	At birth	0.70	0.3–1.5	NA	
Wilkins and Koutras, 1988 (*7*)	Brain	Transportation industry		At birth	1.60	1.0–2.4	97	
		Transportation industry: machine trades occupations			1.00	0.5–2.1	18	
		Transportation industry: motor freight and transportation occupations			1.60	0.9–3.1	37	
		Motor freight and transportation occupations			1.60	0.9–2.7	26	
Howe et al., 1989 (*24*)	Brain	Drivers		Before birth	3.70	0.7–20.7	5	
		Mechanics			0.96	0.2–4.7	4	
Wilkins and Sinks, 1990 (*16*)	Brain	Motor freight and transportation		Preconception	2.30	0.7–8.1	6	
				During pregnancy	1.80	0.6–5.4	7	
				After birth	1.70	0.7–4.5	9	
		Transportation industry		Preconception	1.30	0.6–3.2	13	
				During pregnancy	1.70	0.7–3.9	15	
				After birth	1.20	0.8–1.8	22	
Wilkins and Hundley, 1990 (*25*)	Neuroblastoma	Transportation industry: motor freight and transportation		At birth	0.80	0.4–1.5	18	
					0.80	0.3–1.9	7	

(*Continued*)

Table 2. *Continued.*

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
Olsen et al., 1991 (*23*)	CNS	Auto repair		At time of conception	5.90	S	5	
Kuijten et al., 1992 (*9*)	Brain (astro-cytoma)	Transportation industry		Preconception	0.50	0.2–1.3	21[a]	
				During pregnancy	0.10	0.0–0.6	16[a]	
				After birth	0.60	0.2–1.4	30[a]	
			Motor vehicle exhausts, more exposure	Preconception	0.90	0.4–2.0	32[a]	
				During pregnancy	0.70	0.2–2.6	12[a]	
				After birth	1.00	0.0–78.4	2[a]	
			Motor vehicle exhausts, less exposure	Preconception	0.60	0.3–1.4	32[a]	
				During pregnancy	0.50	0.2–1.3	23[a]	
				After birth	0.70	0.3–1.7	27[a]	

Abbreviations: S, significant; NS, not significant; NA, not available from published report. [a]number of discordant pairs. [ ], calculated by the authors of this review.

No maternal occupation or exposure was consistently associated with childhood nervous system cancers. Findings from individual studies were associations with unspecified chemical exposures (*11*); occupations in which protective clothing or equipment was used (surrogate for exposure) (*26*); unspecified factory work (*24*); nursing (*9*); and slaughterhouses and meat packers, the textile industry, child care workers, and kindergarten teachers (*23*). Savitz and Chen suggested that additional study is needed for unspecified chemical exposures among mothers, but no subsequent studies of this broad exposure have been performed since their review.

Leukemia and Lymphoma

Significant associations have been found in multiple studies for paternal exposure to solvents, paints and pigments, motor vehicle-related occupations, and ionizing radiation (Table 3).

The evidence for an association between childhood leukemia and paternal exposure to solvents is quite strong. All five of the studies addressing solvent exposures have reported positive associations. A number of the relative risks were quite large (i.e., greater than 3.0), and despite the small number of exposed cases in many of the studies, several were statistically significant [solvents in general (*27*), chlorinated solvents (*28*), and benzene, carbon tetrachloride, and trichloroethylene (TCE) (*29*)]. Buckley et al. (*27*) found a significant trend by duration of exposure for unclassified solvents, but could not identify with confidence the specific solvents associated with acute nonlymphocytic leukemia (ANLL) risk. The association between childhood cancer and solvents is an added concern because benzene is a well-established risk factor for adult leukemia and other solvents are suspected leukemogens (*30*).

Several studies have evaluated leukemia risks and paternal exposure to paints and pigments. These occupations may also have solvent exposures. A majority of these studies reported elevated ORs of 1.5 or greater (*12,27,28,31*), with two reaching statistical significance. The two studies that combined leukemia with lymphoma cases found no association (*20,29*). A number of occupational investigations have noted an association between employment as a painter and risk of leukemia (*30*). Savitz and Chen also concluded that exposure to paints and pigments yielded positive results that were relatively consistent and that further investigations were needed.

There have been 12 studies of childhood leukemia and paternal employment in occupations related to motor vehicles or involving exposure to exhaust gases. Elevated risk was found in most of these studies, with statistically significant findings in six. Significant associations were found among diverse occupations such as motor vehicle or lorry drivers (*12,32*), mechanics and gas station attendants (*17,27,33*), and broader groups of motor vehicle-related occupations (*18*). In their review of leukemia, Linet and Cartwright (*30*) suggested that the link between motor vehicle occupations and adult leukemia may be due to benzene and other components in engine exhausts.

Ten studies have examined the relationship between paternal exposure to ionizing radiation and childhood leukemia/lymphoma. For studies that provide results for leukemia alone and for leukemia combined with lymphoma, only the leukemia findings are tabulated. Although the earlier studies found no significant association (*27,31,34*), in 1990 Gardner et al. (*35*) reported that the risk of childhood leukemia in West Cumbria, England, was significantly associated with paternal employment in the Sellafield nuclear fuel reprocessing plant, particularly for fathers with high radiation dose recordings prior to their child's conception. However, the finding was specific to workers in the village of Seascale near Sellafield and was not seen among the offspring of other Sellafield workers with similar preconception doses. McKinney et al. (*29*) and Roman et al. (*36*) also reported significantly increased risks for paternal exposure to ionizing radiation, although the population in McKinney's study overlapped with that of Gardner, and Roman's study was based on small numbers. Four other studies have not provided support for this hypothesis (*37–40*).

Savitz and Chen recommended that paternal HC exposure be studied further in terms of its link with childhood leukemia. With the evidence from more recent investigations, we do not find compelling evidence for this association. As with nervous system cancers, Fabia and Thuy (*17*) were the first to report a significant relationship between hydrocarbon exposure and childhood leukemia. Numerous attempts have been made to replicate these findings (*4,18–20,22,28,31,41*). There have been no significant findings despite a reasonable number of exposed cases. Relative risks were generally close to 1.0. There is a considerable range of possible exposures in this category. This range and the variation in exposure between studies diminishes their value in identifying environmental causes of cancer.

Unlike the nervous system cancers, a variety of maternal occupational exposures have been found to be significantly

Table 3. Childhood leukemia and paternal occupations with significant findings in multiple studies.

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
Solvents								
Buckley et al., 1989 (*27*)	ANLL		Solvents	Ever	2.00	1.2–3.8	57	OR is for highest exposure duration category; *p* trend = 0.003.
				Before pregnancy	2.20	S	NA	
				During pregnancy	2.10	S	NA	
				After birth	1.50	NS	NA	
Feingold et al., 1992 (*22*)	ALL		Solvents	During pregnancy	1.70	0.4–8.2	3	
Shaw et al., 1984 (*54*)	Leukemia		Benzene	At birth	[1.21]	NS	205	
Lowengart et al., 1987 (*28*)	Acute leukemia		Benzene	Year before conception to reference date	NA	NS	NA	
McKinney et al., 1991 (*29*)	Leukemia + NHL		Benzene	Preconception	5.81	1.7–26.4	12	Significance remains after adjustment for other exposures.
				During pregnancy	2.98	0.5–24.2	4	
				After birth	1.39	0.4–4.9	5	
Feingold et al., 1992 (*22*)	ALL		Benzene	During pregnancy	1.60	0.5–5.8	9	
Lowengart et al., 1987 (*28*)	Acute leukemia		Xylene	Year before conception to reference date	NA	NS	NA	
McKinney et al., 1991 (*29*)	Leukemia + NHL		Xylene	Preconception	6.86	0.9–168	5	Not independent of observation for benzene, wood, and radiation.
				During pregnancy	3.24	0.2–98.2	2	
				After birth	3.24	0.2–98.2	2	
Lowengart et al., 1987 (*28*)	Acute leukemia		Toluene	Year before conception to reference date	NA	NS	NA	
			MEK	Year before pregnancy	1.70	NS	8[a]	
				During pregnancy	1.70	NS	8[a]	
				After birth	3.00	0.8–17.2	12[a]	Significant trend with frequency of use ($p=0.03$).
			Chlorinated solvents	Year before pregnancy	2.20	NS	13[a]	
				During pregnancy	2.20	NS	13[a]	
				After birth	3.50	1.1–14.6	18[a]	Significant trend with frequency of use ($p=0.03$). OR retains significance after adjusting for other exposures.
			Carbon tetrachloride	Year before pregnancy	0.70	NS	5[a]	
				During pregnancy	0.70	NS	5[a]	
				After birth	1.70	0.3–10.7	8[a]	
McKinney et al., 1991 (*29*)	Leukemia + NHL		Carbon tetrachloride	Preconception	2.90	1.1–7.4	13	Not independent of observation for benzene, wood, and radiation.
				During pregnancy	2.16	0.5–9.1	5	
				After birth	3.48	0.9–17.2	6	
Lowengart et al., 1987 (*28*)	Acute leukemia		TCE	Year before pregnancy	2.00	NS	9[a]	
				During pregnancy	2.00	NS	9[a]	
				After birth	2.70	0.6–15.6	11[a]	

(*Continued*)

Table 3. *Continued.*

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
McKinney et al., 1991 (*29*)	Leukemia + NHL		TCE	Preconception	2.27	0.8–6.2	9	
				During pregnancy	4.40	1.2–21.0	7	
				After birth	2.66	0.8–9.2	7	
Lowengart et al., 1987 (*28*)	Acute leukemia		PCE	After birth	Infinity	0.2–infinity	2[a]	
Paints and pigments								
Kwa and Fine, 1980 (*20*)	Leukemia + lymphoma	Painters	HCs	At birth	0.90	NS	7	OR calculated by Savitz and Chen (1990) (*2*).
Hemminki et al., 1981 (*12*)	Leukemia	Painters		During pregnancy	1.50	NS	12[a]	
Van Steensel-Moll et al., 1985 (*31*)	ALL		Pigment (dyes)	During pregnancy	1.60	0.8–3.3	25	
Lowengart et al., 1987 (*28*)	Acute leukemia		Spray paint	Year before pregnancy	1.40	NS	31[a]	
				During pregnancy	2.20	S	26[a]	Loses significance when adjusted for chlorinated solvents.
				After birth	2.00	0.96–4.4	36[a]	Significant trend with frequency of use ($p = 0.01$). Loses significance when adjusted for chlorinated solvents.
			Dyes, pigments	Year before pregnancy	3.50	NS	9[a]	
				During pregnancy	3.00	NS	8[a]	
				After birth	4.50	0.9–42.8	11[a]	Significant trend with frequency of use ($p = 0.04$). Loses significance when adjusted for chlorinated solvents.
Buckley et al., 1989 (*27*)	ANLL	Painters		Ever	7.00	S	7	
McKinney et al., 1991 (*29*)	Leukemia + NHL		Paints and dyes		NA	NS	NA	Authors say "failed to confirm association."
Motor vehicle-related occupations								
Fabia and Thuy, 1974 (*17*)	Leukemia + lymphoma	Motor vehicle mechanic, service station attendant	HCs	At birth	[2.03]	S	16	
Hakulinen et al., 1976 (*19*)	Leukemia + lymphoma	Motor vehicle drivers	HCs	During pregnancy	1.06	0.6–1.8	[35]	
Kwa and Fine, 1980 (*20*)	Leukemia + lymphoma	Mechanics, gas station attendants	HCs	At birth	1.10	NS	21	ORs calculated by Savitz and Chen (1990) (*2*).
		Motor vehicle drivers			1.00	NS	28	
Hemminki et al., 1981 (*12*)	Leukemia	Motor vehicle drivers		During pregnancy	1.50	NS	96[a]	Results are for entire study period.
					1.90	S	45[a]	Results are for 1969–1975 only.
Gold et al., 1982 (*18*)	Leukemia	Motor vehicle related (driver, mechanic, service station attendant, railroad worker/engineer)		Before birth	0.75	NS	7[a]	Results are for healthy controls.
					Infinity	S	6[a]	Results are for cancer controls.
		Drivers		After birth	1.50	NS	10[a]	Results are for healthy controls.
					6.00	NS	7[a]	Results are for cancer controls.
Vianna et al., 1984 (*33*)	Acute leukemia	High: gas station attendants, auto or truck repairmen, aircraft maintenance	Motor vehicle exhaust	Before birth	2.43	S	24[a]	Results are for control group A.

(*Continued on next page*)

Table 3. *Continued.*

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
Vianna et al., 1984 (*33*)	Acute leukemia				2.50	S	28[a]	Results are for control group B.
		Moderate: cab driver, traveling salesman, truck or bus driver, railroad worker, toll booth attendant, highway worker, police officer	Motor vehicle exhaust	Before birth	1.27	NS	25[a]	Results are for control group A.
					3.75	S	19[a]	Results are for control group B.
Van Steensel-Moll et al., 1985 (*31*)	ALL		Exhaust gases	During pregnancy	1.30	0.8–1.9	89	
Shu et al., 1988 (*43*)	Leukemia	Transportation equipment operator		During pregnancy	1.20	0.6–2.3	24	
Buckley et al., 1989 (*27*)	ANLL	Nonauto mechanics		Ever	3.50	S	14	
Magnani et al., 1990 (*32*)	NHL	Lorry driver		Before birth	5.00	1.1–22.4	2	
				After birth	5.00	1.1–22.4	2	
McKinney et al., 1991 (*29*)	Leukemia + NHL		Exhaust fumes		NA	NS	NA	
Roman et al., 1993 (*36*)	Leukemia + NHL	Drivers and related		At birth	0.60	0.1–2.0	3	
				Before birth through diagnosis	1.30	0.4–3.2	7	
Ionizing radiation								
Hicks et al., 1984 (*34*)	Leukemia + NHL	Occupations	Ionizing radiation	Year before birth	0.78–1.41	NS	10–27	Range of ORs for different control groups and exposure intensities.
		Industries	Ionizing radiation		0.76–1.09	NS	8–42	Range of ORs for different control groups and exposure intensities.
Van Steensel-Moll et al., 1985 (*31*)	Leukemia		Radioactivity	During pregnancy	1.40	0.6–3.5	13	
Buckley et al., 1989 (*27*)	Leukemia		Ionizing radiation	Ever	1.90	NS	17	
Gardner et al., 1990 (*35*)	Leukemia	Nuclear plant		At birth	2.82	1.1–7.4	9	Area controls.
					2.03	0.7–5.9	9	Local controls.
			External ionizing radiation	Preconception	6.24	1.5–25.8	4	For external radiation doses exceeding 100 mSv. Area controls.
					8.38	1.4–52.0	4	For external radiation doses exceeding 100 mSv. Local controls.
Urquhart et al., 1991 (*37*)	Leukemia + NHL	Nuclear industry	Radiation	At conception	0.58	0.1–2.6	3	
McKinney et al., 1991 (*29*)	Leukemia + NHL		Radiation	Preconception	3.23	1.4–7.7	15	Study population overlaps with Gardner et al. (1990) (*35*).
				During pregnancy	15.06	2.4–338	8	
				After birth	3.08	1.01–10.3	9	
Kinlen et al., 1993 (*38*)	Leukemia	Nuclear industry	Ionizing radiation	Preconception	1.26	0.6–3.9	11	
Roman et al., 1993 (*36*)	Leukemia + NHL	Nuclear industry		Ever	2.50	0.6–9.0	4	
				Preconception	2.80	0.6–10.5	4	
			Monitored for radiation exposure	Ever	8.00	1.4–54.6	4	
				Preconception	9.00	1.0–107.8	3	
McLaughlin et al., 1993 (*39*)	Leukemia	Nuclear industry (predominantly)	Radiation	Preconception	0.87	0.2–2.3	6	
Sorahan et al., 1993 (*40*)	Leukemia		External ionizing radiation	Preconception	1.45	0.8–2.8	29	
			Radionuclides		2.75	0.9–8.6	11	.

NA, Not available from published report; S, significant; NS, not significant. [a]Total number of discordant pairs. [ ], calculated by the authors of this review.

associated with childhood leukemia, including personal services, textiles, and metals (Table 4). All four studies that looked at mothers employed in the personal services industry found significant associations with childhood leukemia. The specific occupations held by the mothers, however, were heterogeneous. In Lowengart's study (*28*), mothers in the personal services industry were employed in beauty shops, as domestics in personal households or other lodgings, or in laundries. Van Steensel-Moll et al. (*31*) focused on domestics and hotel and catering employees. Magnani et al. (*32*) observed excesses among cleaners; McKinney et al. (*29*) had a category of catering, cleaning, and hairdressing. The presence of significant associations between leukemia and employment in the personal services industry before birth, but not during the postnatal period, may provide an important mechanistic lead.

Three of the four studies that presented data on the textile industry found significant risks for childhood leukemia (*31,32,42*). Numbers of exposed cases were small, but relative risks were large. This lead could be especially important given the large number of women employed in the textile industry in many countries. Only two studies addressed maternal employment in occupations likely to involve exposure to metals, and both found significantly elevated risks (*27,43*). As with nervous system cancers, Savitz and Chen suggested that additional study is needed for leukemia and unspecified chemical exposures among mothers, but no additional studies have taken place since their review.

Urinary System Cancers

Savitz and Chen did not point to any specific paternal exposures warranting further study for urinary tract cancers and only one study of urinary system cancers has been published since their review. The only exposure with a significant finding in more than one study is HCs (Table 5). With the possible exception of Bunin et al. (*44*) (for which no odds ratio was provided), the studies consistently reported elevated risk from HC exposure, although the differences are not always statistically significant. Aromatic HCs have been clearly established risk factors for adult kidney cancer in studies of coke-oven workers (*45*).

Kantor et al. (*46*) observed an increased risk for Wilms tumor that they attributed to lead. Other studies (*44,47,48*) have investigated lead as a possible etiologic

Table 4. Childhood leukemia and maternal occupations/exposures with significant findings in multiple studies.

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
Personal services								
Van Steensel-Moll et al., 1985 (*31*)	ALL	Domestics, hotel, catering		During pregnancy	2.80	1.3–5.7	24	
				After birth	1.90	0.8–4.6	15	
Lowengart et al., 1987 (*28*)	Acute leukemia	Personal services industry (beauty shops, domestics, laundries)		Year before conception to after birth	2.70	S	12	
Magnani et al., 1990 (*32*)	ALL	Cleaner		Before birth	3.00	1.1–8.4	8	
				After birth	0.60	0.1–3.0	2	
McKinney et al., 1991 (*29*)	Leukemia + NHL	Catering, cleaning, hairdressing		Preconception	2.84	1.6–5.2	38	
				During pregnancy	3.12	1.1–8.7		
Textiles								
Van Steensel-Moll et al., 1985 (*31*)	ALL	Textile industry		During pregnancy	4.20	1.0–17.7	8	
Shu et al., 1988 (*43*)	Leukemia	Textile workers and tailors		During pregnancy	0.70	0.4–1.2	27	
Magnani et al., 1990 (*32*)	ANLL	Textile spinner and winder		Before birth	10.10	2.2–46.0	2	
				After birth	10.10	2.2–46.0	2	
		Textile industry		Before birth	1.90	0.5–6.6	3	
				After birth	4.30	1.2–15.0	3	
Infante-Rivard et al., 1991 (*42*)	ALL	Sewing at home	Dust (cotton, wool, synthetic fibers)	During pregnancy	5.50	1.2–24.8	12	
Metals								
Shu et al., 1988 (*43*)	Leukemia	Metal refining and processing workers		During pregnancy	2.60	0.9–7.7	8	
	ALL				1.00	0.2–4.9	2	
	ANLL				4.60	1.3–17.2	5	
	Leukemia		Lead		1.90	0.5–6.9	5	
Buckley et al., 1989 (*27*)	ANLL	Metal manufacturing		Ever	4.50	S	10	Significant trend by duration of exposure.
			Metal dusts	Before pregnancy	5.50	S	NA	
				During pregnancy	3.00	NS	NA	
				After birth	1.50	NS	NA	

Abbreviations: NA, not available from published report; S, significant; NS, not significant agent for Wilms tumor but have not replicated the Kantor et al. (*46*) finding. Although lead causes cancer in experimental animals, the epidemiologic evidence is weak (*49*). In the only study published since Savitz and Chen's review, significant associations were found between renal cancers and paternal employment in general manufacturing, the wood and furniture industry, manufacturing of iron and metal structures, and electrical contracting firms (*23*).

Only two studies have looked at maternal occupations and childhood urinary tract cancers. There have been isolated significant findings for Wilms tumor and maternal exposure to aromatic amines (*44*); and for renal cancer and education, health and welfare, health departments, and practicing dentists (*23*).

Discussion

Although several occupation/cancer combinations are intriguing and clearly deserve further attention, the evidence for any association falls short of certainty. The strongest evidence for an association between fathers' occupations and the risk of childhood cancer is for exposure to solvents and paints and the risk of leukemias and cancers of the nervous system. These associations are biologically plausible given findings from experimental investigations and epidemiologic studies of adult cancer (*49*).

For nervous system cancers, the evidence is less convincing for other paternal occupations. Despite the large number of positive findings in EMF studies, investigators have hesitated to conclude that the association is real. The biologic plausibility is uncertain (*25*) and the findings are inconsistent for direct exposures to children as well as adults. It is also possible that positive findings are indicative of exposures other than EMF in these occupations. Employment in the electrical or electronics industry may entail exposure to various chemicals including solvents, soldering fumes, epoxy, phenolic resins, polychlorinated biphenyls, and metals (beryllium, nickel, lead, zinc, platinum, tellurium) (*7,8,25*).

Epidemiologic studies provide strong evidence for a link between childhood leukemia and paternal exposure to solvents. This is consistent with other experimental findings and epidemiologic studies among adults (*49*). Children may be exposed to solvents that their parents bring home from the workplace on their skin or clothes, or from their exhaled air. Chlorinated solvents have been found in the exhaled air of workers a number of hours after exposure, and perchloroethylene was detected in the breast milk and blood of a mother who visited her husband daily at a dry cleaning establishment (*28*).

Painters, printers, and workers in motor vehicle-related occupations, which are fairly consistently linked with childhood leukemia, may have occupational exposure to solvents. Painters are typically exposed to a number of different solvents (*28*), and workers in motor vehicle-related occupations (mechanics, gas station attendants, drivers) are exposed to gasoline and gasoline exhaust, which contain benzene (*22,29,43*). However, these occupations involve exposure to a variety of other chemicals as well. For example, gasoline contains dichloroethane and dibromomethane (*12*), and the particulate fraction of exhaust fumes contains aromatic compounds such as benzo[*a*]pyrene that are capable of producing tumors in lower animals (*33*).

Although there is strong evidence that children directly exposed to ionizing radiation are at increased risk for developing leukemia, the evidence for a link between childhood leukemia and paternal radiation exposure is weak. Gardner et al. (*35*) were the first to report such an association, but the elevated risk among Sellafield plant workers was found only among those living in one particular villlage. McKinney's study population (*29*) overlapped with that of Gardner's, and Roman's results (*36*) were based on a small number of cases. Most of the studies have not found an association. In a review of this topic, Little et al. (*50*) and Doll et al. (*51*) concluded that the inconsistency not only with other epidemiologic data but also with experimental data makes it highly unlikely

Table 5. Childhood urinary tract cancers and paternal occupations with significant findings in multiple studies.

Reference	Histology	Industry or occupation	Exposure	Time frame	Relative risk	95% CI	Number of exposed cases	Comments
Hydrocarbons								
Kantor et al., 1979 (*46*)	Wilms	Machinist, cleaner, embalmer, driver, motor vehicle mechanic, service station attendant	HCs (some also involve lead)	At birth	2.40	1.1–5.7	24	The authors conclude that increased risk is due to lead rather than HCs.
		Machinist, cleaner, embalmer	HCs only		1.40	NS	7	
		Driver, motor vehicle mechanic, service station attendant	HCs and lead		3.40	NS	17	
Kwa and Fine, 1980 (*20*)	Urinary tract	Mechanics, gas station attendants, machinists	HCs		2.50	S	10	
Sanders at al., 1981 (*4*)	Kidney	Miners, engineering and allied trades, textile workers,printers, painters,decorators, dry cleaners, motor vehicle drivers	HCs	At child's death	1.19	NS	79	
Wilkins and Sinks, 1984 (*47*)	Wilms	Motor vehicle mechanic, service station attendant, driver/heavy equipment operator, metal worker/machinist, lumberman, miner, painter, printer, leather worker, factory worker	HCs	At birth	1.4	0.7–2.7	19	
Bunin et al., 1989 (*44*)	Wilms		HCs	Age 18–after birth	NA	NS	NA	

that the association observed in Gardner's study represents a causal relationship. Studies have not shown elevated leukemia risks among children of atomic bomb survivors, although the relationship between paternal irradiation prior to conception and cancer in the offspring has not been well studied in this cohort.

Studies of maternal occupations raise the possibility that mothers employed in personal services and textiles occupations may place their children at increased risk for leukemia. The specific exposures that may be responsible are unknown. Personal services occupations are heterogeneous. Women in the textile industry may be exposed to a variety of substances including organic dusts and fibers, dyes in synthetic fibers, and oil, grease, and EMF from their sewing machines (*42,52*). These findings need further evaluation, given the large number of women employed in these industries.

Results from studies of childhood cancer and parental occupation must be evaluated in light of their strengths and weaknesses. Epidemiologic studies of parental occupation and childhood cancer face many of the same methodological challenges as studies of adult occupation and cancer. In particular, assessing exposures to specific workplace agents is problematic when the only available information is a job or industry title, as is the case with virtually all of the childhood cancer studies conducted to date. Workers with identical job titles can have vastly different exposures depending on their specific activities and the extent to which exposure controls (e.g., protective equipment, ventilation) are used. The impact on estimates of relative risk from reliance on simple and less accurate exposure assessment procedures is clear: it would tend to bias estimates of relative risks toward the null (*53*). An additional limitation of the use of simple, qualitative exposure assessments is that it is more difficult to evaluate exposure–response relationships, a key criterion for the assessment of causality.

Exposure assessment in childhood cancer studies is further hampered by our lack of understanding regarding the relevant time frame of exposure. In most circumstances we do not know whether exposures relevant to the disease process occur prior to conception (i.e., germ cell effects), during pregnancy (i.e., transplacentally, from exposures experienced by the mother at the workplace or from paternal transfer of substances from the workplace to the home), or after birth (i.e., substances carried home by either parent). Studies should be designed to focus on all three time periods. Little is known about the effectiveness of transplacental exposures or on the transfer of chemicals from the workplace to the home. It surely varies by type of parental exposure and by workplace practices such as showering or changing back to street clothes before going home, yet these factors have not been taken into account in any of the studies so far. On the other hand, although the relevant time frame of exposure is uncertain for children, it is likely narrower than it is for adults, which makes exposure assessment easier. Except for the preconception mechanisms, childhood cancer involves exposure for at most a couple of decades (i.e., from conception to the late teenage years), whereas the relevant exposure time frame for adult cancers typically spans several decades. If the relevant exposures are preconceptional (germ cell effects), the time frame can, of course, be as long as the parent's life, or may even extend to the prenatal period for the mother.

Small numbers of exposed cases in studies of occupation and child cancer make it difficult to achieve stable results. Some investigators have addressed this problem by aggregating different jobs believed to have common exposures. This approach can increase numbers and lead to more stable results, and also minimizes contamination of the unexposed group with jobs that have the exposure of interest. On the other hand, it may increase misclassification of exposure by combining jobs with different exposures (*2*).

As with studies of adult cancer and occupation, as the number of studies and comparisons increases, the number of significantly elevated relative risks that are due strictly to chance also increases. Evaluation of consistency across studies, however, tends to address this issue. A false impression of a positive association could also arise because of selective reporting of study results by authors. In each of the 48 studies reviewed here, it was possible to evaluate childhood cancer risks from parental employment in numerous occupations and from exposure to a variety of substances. Only a small number of these comparisons, however, is reported in any paper. Thus, selective reporting is occurring. It seems reasonable to assume that authors may tend to preferentially report positive findings. With such a bias, the literature may appear more consistently positive than appropriate.

Despite these limitations, epidemiologic studies have provided sufficient evidence that certain parental exposures may be harmful to their children. Paternal exposures to paints (nervous system cancers and leukemia), solvents (leukemia), and employment in motor vehicle-related occupations (leukemia) clearly deserve further study. To more clearly evaluate the importance of these and other exposures, more sophisticated assessment approaches need to be employed in future investigations. Improvements are needed in four areas. First, more careful attention must be paid to maternal exposures because of the potential for transfer of chemicals to the child during pregnancy and nursing. Second, studies must employ sophisticated exposure assessment techniques capable of developing quantitative estimates of specific chemicals. Third, careful attention must be paid to the postulated mechanism and route of exposure. To the extent possible, exposures should be assessed specifically for the preconception, prenatal, and postnatal periods. Finally, if postnatal exposures are evaluated, studies need to provide evidence that the exposure is actually transferred from the workplace to the child's environment.

REFERENCES AND NOTES

1. Ries LAG, Kosary CL, Hankey BF, Miller BA, Harras A, Edwards B (eds). SEER Cancer Statistics Review, 1973-1994. NIH Publ 97-2789. Bethesda, MD:National Cancer Institute, 1997.
2. Savitz DA, Chen J. Parental occupation and childhood cancer: review of epidemiologic studies. Environ Health Perspect 88:325–337 (1990).
3. Zahm SH, Ward MH. Pesticides and childhood cancer. Environ Health Perspect 102(Suppl 3):893–908 (1998).
4. Sanders BM, White GC, Draper GJ. Occupations of fathers of children dying from neoplasms. J Epidemiol Comm Health 35: 245–250 (1981).
5. Wilkins JR, McLaughlin JA, Sinks TH, Kosnik EJ. Parental occupation and intracranial neoplasms of childhood: anecdotal

evidence from a unique occupational cancer cluster. Am J Ind Med 19:643–653 (1991).
6. Spitz MR, Johnson CC. Neuroblastoma and paternal occupation, a case-control analysis. Am J Epidemiol 121:924–929 (1985).
7. Wilkins JR, Koutras RA. Paternal occupation and brain cancer in offspring: a mortality-based case-control study. Am J Ind Med 14:299–318 (1988).
8. Johnson CC, Spitz MR. Childhood nervous system tumors: an assessment of risk associated with paternal occupations involving use, repair, or manufacture of electrical and electronic equipment. Int J Epidemiol 18:756–762 (1989).
9. Kuijten RR, Bunin GR, Nass CC, Meadows AT. Parental occupation and childhood astrocytoma: results of a case-control study. Cancer Res 52:782–786 (1992).
10. Preston-Martin S, Mack T. Neoplasms of the nervous system. In: Cancer Epidemiology and Prevention (Schottenfeld D, Fraumeni JF Jr, eds). New York:Oxford University Press, 1996; 1231–1281.
11. Peters JM, Preston-Martin S, Yu MC. Brain tumors in children and occupational exposure of parents. Science 213:235–247 (1981).
12. Hemminki K, Saloniemi S, Salonen T, Partanen T, Vainio H. Childhood cancer and parental occupation in Finland. J Epidemiol Comm Health 35:11–15 (1981).
13. Johnson CC, Annegers JF, Frankowski RF, Spitz MR, Buffler PA. Childhood nervous system tumors—an evaluation of the association with paternal occupational exposure to hydrocarbons. Am J Epidemiol 126:605–613 (1987).
14. Heineman EF, Cocco P, Gomez MR, Dosemeci M, Stewart PA, Hayes RB, Zahm SH, Thomas TL, Blair A. Occupational exposure to chlorinated aliphatic hydrocarbons and risk of astrocytic brain cancer. Am J Ind Med 26:155–169 (1994).
15. Baker EL. A review of recent research on health effects of human occupational exposure to organic solvents. J Occup Med 36:1079–1082 (1994).
16. Wilkins JR, Sinks T. Parental occupation and intracranial neoplasms of childhood: results of a case-control study. Am J Epidemiol 132:275–292 (1990).
17. Fabia J, Thuy TD. Occupation of father at time of birth of children dying of malignant diseases. Br J Prev Soc Med 28: 98–100 (1974).
18. Gold EB, Diener MD, Szklo M. Parental occupations and cancer in children. J Occup Med 24:578–584 (1982).
19. Hakulinen T, Salonen T, Teppo L. Cancer in the offspring of fathers in hydrocarbon-related occupations. Br J Prev Soc Med 30:138–140 (1976).
20. Kwa SL, Fine LJ. The association between parental occupation and childhood malignancy. J Occup Med 22:792–794 (1980).
21. Nasca PC, Baptiste MS, MacCubbin PA, Metzger BB, Carlton K, Greenwald P, Armbrustmacher VW, Earle KM, Waldman J. An epidemiologic case-control study of central nervous system tumors in children and parental occupational exposures. Am J Epidemiol 128:1256–1265 (1988).
22. Feingold L, Savitz DA, John EM. Use of a job-exposure matrix to evaluate parental occupation and childhood cancer. Cancer Causes Control 3:161–169 (1992).
23. Olsen JH, Brown PdN, Schulgen G, Jensen OM. Paternal employment at time of conception and risk of cancer in offspring. Eur J Cancer 27:958–965 (1991).
24. Howe GR, Burch JD, Chiarelli AM, Risch HA, Choi BCK. An exploratory case-control study of brain tumors in children. Cancer Res 49:4349–4352 (1989).
25. Wilkins JR, Hundley VD. Paternal occupational exposure to electromagnetic fields and neuroblastoma in offspring. Am J Epidemiol 131:995–1008 (1990).
26. Preston-Martin S, Yu MC, Benton B, Henderson BE. *N*-Nitroso compounds and childhood brain tumors: a case-control study. Cancer Res 42:5240–5245 (1982).
27. Buckley JD, Robison LL, Swotinsky R, Garabrant DH, LeBeau M, Manchester P, Nesbit ME, Odom L, Peters JM, Woods WG, et al. Occupational exposures of parents of children with acute nonlymphocytic leukemia: a report from the Childrens Cancer Study Group. Cancer Res 49:4030–4037 (1989).
28. Lowengart RA, Peters JM, Ciconi C, Buckley J, Bernstein L, Preston-Martin S, Rappaport E. Childhood leukemia and parents' occupational and home exposures. J Natl Cancer Inst 79: 39–46 (1987).
29. McKinney PA, Alexander FE, Cartwright RA, Parker L. Parental occupations of children with leukemia in west Cumbria, north Humberside, and Gateshead. Br Med J 302: 681–687 (1991).
30. Linet MS, Cartwright RA. The leukemias. In: Cancer Epidemiology and Prevention (Schottenfeld D, Fraumeni JF Jr, eds). New York:Oxford University Press, 1996;841–892.
31. Van Steensel-Moll HA, Valkenburh HA, Van Zanen GE. Childhood leukemia and parental occupation, a register-based case-control study. Am J Epidemiol 121:216–224 (1985).
32. Magnani C, Pastore G, Luzzato L, Terracini B. Parental occupation and other environmental factors in the etiology of leukemias and non-Hodgkin's lymphomas in childhood: a case-control study. Tumori 76:413–419 (1990).
33. Vianna NJ, Kovasznay B, Polan A, Ju C. Infant leukemia and paternal exposure to motor vehicle exhaust fumes. J Occup Med 26:679–681 (1984).
34. Hicks N, Zack M, Caldwell GG, Fernbach DJ, Falletta JM. Childhood cancer and occupational radiation exposure in parents. Cancer 53:1637–1643 (1984).
35. Gardner MJ, Snee MP, Hall AJ, Powell CA, Downes S, Terrell JD. Results of case-control study of leukemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria. Br Med J 300:423–429 (1990).
36. Roman E, Watson A, Beral V, Buckle S, Bull D, Baker K, Ryder H, Barton C. Case-control study of leukemia and non-Hodgkin's lymphoma among children aged 0-4 years living in West Berkshire and North Hampshire health districts. Br Med J 306:615–621 (1993).
37. Urquhart JD, Black RJ, Muirhead MJ, Sharp L, Maxwell M, Eden OB, Jones DA. Case-control study of leukemia and non-Hodgkin's lymphoma in children in Caithness near the Dounreay nuclear installation. Br Med J 302:687–692 (1991).
38. Kinlen LJ, Clarke K, Balkwill A. Paternal preconceptional radiation exposure in the nuclear industry and leukaemia and non-Hodgkin's lymphoma in young people in Scotland. Br Med J 306:1152–1158 (1993).
39. McLaughlin JR, King WD, Anderson TW, Clarke EA, Ashmore JP. Paternal radiation exposure and leukaemia in offspring: the Ontario case-control study. Br Med J 307:959–966 (1993).
40. Sorahan T, Roberts PJ. Childhood cancer and paternal exposure to ionizing radiation: preliminary findings from the Oxford survey of childhood cancers. Am J Ind Med 23: 343–354 (1993).
41. Zack M, Cannon S, Loyd D, Heath CW, Falletta JM, Jones B, Housworth J, Crowley S. Cancer in children of parents exposed to hydrocarbon-related industries and occupations. Am J Epidemiol 111:329–336 (1980).
42. Infante-Rivard C, Mur P, Armstrong B, Alvarez-Dardet C, Bolumar F. Acute lymphoblastic leukemia among Spanish children and mothers' occupation: a case-control study. J Epidemiol Comm Health 45:11–15 (1991).
43. Shu XO, Gao YT, Brinton LA, Linet MS, Tu JT, Zheng W, Fraumeni JF. A population-based case-control study of childhood leukemia in Shanghai. Cancer 62:635–644 (1988).
44. Bunin GR, Nass CC, Kramer S, Meadows AT. Parental occupation and Wilms' tumor: results of a case-control study. Cancer Res 49:725–729 (1989).
45. McLaughlin JK, Blot WJ, Devesa SS, Fraumeni JF Jr. Renal cancer. In: Cancer Epidemiology and Prevention (Schottenfeld D, Fraumeni JF Jr, eds). New York:Oxford University Press, 1996;1142–1155.
46. Kantor AF, Curnen MGM, Meigs JW, Flannery JT. Occupations of fathers of patients with Wilms' tumour. J Epidemiol Comm Health 33:253–256 (1979).

47. Wilkins JR, Sinks TH. Paternal occupation and Wilms' tumour in offspring. J Epidem Comm Health 38:7–11 (1984a).
48. Wilkins JR, Sinks TH. Occupational exposures among fathers of children with Wilms' tumour. J Occup Med 26:427–435 (1984b).
49. IARC. Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs, Volumes 1 to 42. Suppl 7. Lyon, International Agency for Research on Cancer, 1987.
50. Little MP, Charles MW, Wakeford R. A review of the risks of leukaemia in relation to parental pre-conception exposure to radiation. Health Phys 68:299–310 (1995).
51. Doll R, Evans HJ, Darby SC. Paternal exposure not to blame. Nature 367:678–680 (1994).
52. Infante-Rivard C. Electromagnetic field exposure during pregnancy and childhood leukaemia [Letter to the Editor]. Lancet 346:177 (1995).
53. Checkoway H, Pearce NE, Crawford-Brown DJ. Research Methods in Occupational Epidemiology. New York:Oxford University Press, 1989.
54. Shaw G, Lavey R, Jackson R, Austin D. Association of childhood leukemia with maternal age, birth order, and paternal occupation, a case-control study. Am J Epidemiol 119:788–795 (1984).
55. Olshan AF, Breslow NE, Daling JR, Weiss NS, Leviton A. Childhood brain tumors and paternal occupation in the aerospace industry. J Natl Cancer Inst 77:17–19 (1986).
56. Gold E, Gordis L, Tonascia J, Szklo M. Risk factors for brain tumors in children. Am J Epidemiol 109:309–319 (1979).
57. Bunin GR, Ward E, Kramer S, Rhee CA, Meadows AT. Neuroblastoma and parental occupation. Am J Epidemiol 131: 776–780 (1990).
58. Bunin GR, Petrakova A, Meadows AT, Emanuel BS, Buckley JD, Woods WG, Hammond GD. Occupations of parents of children with retinoblastoma: a report from the Children's Cancer Study Group. Cancer Res 50:7129–7133 (1990).
59. Sorahan T, Lancashire RJ, Temperton DH, Heighway WP. Childhood cancer and paternal exposure to ionizing radiation: a second report from the Oxford survey of childhood cancers. Am J Ind Med 28:71–78 (1995).
60. Wilkins JR, Wellage LC. Brain tumor risk in offspring of men occupationally exposed to electric and magnetic fields. Scand J Work Environ Health 22:339–345 (1996).
61. Gelberg KH, Fitzgerald EF, Hwang S-A, Dubrow R. Growth and development and other risk factors for osteosarcoma in children and young adults. Int J Epidemiol 26:272–278 (1997).