Parental Occupational Exposures and Risk of Childhood Cancer

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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 the 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...
### 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) review | | | | | | Total cancer, leukemia + lymphoma, nervous system, Wilms |
| Fabia and Thuy, 1974 (17) | Birth certificates + IH assessment | At birth | 4 | Mortality | Father | Total cancer, leukemia + lymphoma, nervous system, Wilms |
| Kantor et al., 1973 (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, urinaiy system |
| Zack et al., 1980 (47) | Questionnaire + IH assessment | Year before birth, at birth, after birth | 15 | Incidence | Father | Total cancer, leukemia + lymphoma, nervous system, Wilms |
| Peters et al., 1981 (17) | 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 (16) | 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 (47) classification | At birth | NA | Incidence | Father | Wilms |
| Wilkins and Sinks, 1984 (49) | 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 (47) 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 (26) | 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 (27) | Questionnaire + Zack (47), 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 (6) | 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., 1991 (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 |
| Kujten 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 (38) | 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, after birth | 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 postnatal). Overall, the preconception, pregnancy, and postnatal periods receive 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 |
|-----------|-----------|------------------------|----------|------------|--------------|--------|------------------------|----------|
| Spitz and Johnson, 1985 (6) | Neuroblastoma | 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 | At birth | 2.13 | 1.05–4.4 | 17 | |
| Wilkins and Koutras, 1988 (7) | Brain | Structural work: electrical assembling, installation, and repair occupations | EMF | At birth | 11.75 | 1.4–98.6 | 6 | |
| | | Machinery industry: electrical assembly, installation, repair occupations | EMF | At birth | 2.70 | 1.2–6.1 | 19 | |
| Nasca et al., 1988 (21) | Nervous system | Electricians, electronics workers, power linemen, electrical equipment repairmen, utility workers | EMF | At birth | 1.70 | 0.8–3.6 | 15 | |
| Johnson and Spitz, 1989 (8) | Central nervous system | Industries: Electronics manufacturing | EMF | At birth | 1.64 | 0.96–2.8 | 25 | |
| | | Computer and office machine manufacturing | EMF | At diagnosis | 3.56 | 1.04–12.2 | 7 | |
| | | Refrigeration and air conditioning manufacturing | EMF | At birth | 4.07 | 0.7–22.3 | 4 | |
| | | Electrical and electronic apparatus manufacturing | EMF | At diagnosis | 1.36 | 0.2–8.2 | 2 | |
| | | Electronic components manufacturing | EMF | At birth | 1.22 | 0.3–5.1 | 3 | |
| | | Telephone communications | EMF | At diagnosis | 2.71 | 0.6–12.2 | 4 | |
| | | Electric utilities | EMF | At diagnosis | 1.63 | 0.4–6.1 | 4 | |
| | | Electric repair | EMF | At diagnosis | 1.44 | 0.9–2.4 | 28 | |
| | | Occupations | EMF | At diagnosis | 2.01 | 0.3–14.3 | 2 | |
| | | Radio operators | EMF | At diagnosis | 1.01 | 0.2–5.5 | 2 | |
| | | Electrical goods and appliance salesmen | EMF | At diagnosis | 2.68 | 0.6–12.0 | 4 | |
| | | Computer and business machine, power plant, utilities service mechanics | EMF | At diagnosis | 3.52 | 1.02–12.1 | 7 | |
| | | Electrical and electronics assemblers and mechanics | EMF | At diagnosis | 10.05 | 1.2–90.3 | 5 | |
| Bunin et al., 1990 (57) | Neuroblastoma | Electricians; electrical and electronic workers; linemen, welders, utility employees | EMF | Preconception | 1.30 | 0.4–4.1 | 16a | |
| | | During pregnancy | EMF | Preconception | 0.30 | 0.1–1.3 | 12a | |
| | | Electricians; electrical and electronic workers; linemen, welders, utility employees, electrical equipment salesmen and repairmen | EMF | Preconception | 1.00 | 0.4–2.3 | 28a | |
| | | During pregnancy | EMF | Preconception | 0.60 | 0.2–1.6 | 19a | |
| | | Electrical and electronic products workers | EMF | Preconception | 1.60 | 0.5–6.2 | 13a | |
| | | Electrical and electronic products assemblers | EMF | Preconception | 4.00 | 0.4–195 | 5a | |

(Continued on next page)
| Reference               | Histology     | Industry or occupation | Exposure          | Time frame       | Relative risk | 95% CI  | Number of exposed cases | Comments                                      |
|------------------------|---------------|------------------------|-------------------|------------------|---------------|---------|------------------------|-----------------------------------------------|
| Wilkins and Hundle,    | Neuro-         | Different clustering   | EMF               | At birth         | 0.5–1.9       | NS      | 4–24                   |                                               |
| 1990 (25)              | blastoma      | schemes                |                   |                  |               |         |                        |                                               |
| Wilkins et al.,        | Brain         | Electronic components  |                   | 73.30            | 26.5–157.5    | 6       |                        | Standardized incidence ratio for possible     |
| 1991 (5)               | Brain         | manufacturer            |                   |                  |               |         |                        | cancer cluster                                |
| Kuijten et al.,        | Brain         | Electrical assembling, | EMF               | Preconception    | 1.00          | 0.4–2.8 | 18*                   |                                               |
| 1992 (9)               | (astrocytoma) | installing, repair      |                   |                  |               |         |                        |                                               |
|                        | Brain         | Electrical repair only  |                   | During pregnancy | 1.00          | 0.3–3.7 | 12*                   |                                               |
|                        | Brain         | EMF (definite)         |                   |                  |               |         |                        |                                               |
|                        | Brain         | EMF (probable)         |                   |                  |               |         |                        |                                               |
| Wilkins and Wellage,   | Brain         | EMF                    |                   |                  |               |         |                        |                                               |
| 1996 (60)              | (probable)    |                        |                   |                  |               |         |                        |                                               |
| Paints and pigments    | Nervous       | Painters               |                   |                  |               |         |                        |                                               |
| Kwa and Fine, 1980 (20) | system       |                        |                   |                  |               |         |                        |                                               |
| Peters et al., 1981 (11)| Brain        | Painters               |                   |                  |               |         |                        |                                               |
| Hemminki et al., 1981 (12)| Brain    | Painter                |                   |                  |               |         |                        |                                               |
| Johnson et al., 1987 (13)| Nervous  | Printers               |                   |                  |               |         |                        |                                               |
|                        | system       |                        |                   |                  |               |         |                        |                                               |
|                        | Nervous       | Printing workers       |                   |                  |               |         |                        |                                               |
|                        | system       | Graphic arts workers   |                   |                  |               |         |                        |                                               |
|                        | Nervous       | Newspaper and          |                   |                  |               |         |                        |                                               |
|                        | system       | printing industries    |                   |                  |               |         |                        |                                               |
| Kuijten et al., 1992 (9)| Brain        | Newspaper and          |                   |                  |               |         |                        |                                               |
|                        | (astrocytoma) | printing industry      |                   |                  |               |         |                        |                                               |
|                        | Paint        | Printing workers       |                   |                  |               |         |                        |                                               |
| Hydrocarbons           | Nervous       | Motor vehicle mechanic |                   |                  |               |         |                        |                                               |
| Fabia and Thuy, 1974 (17)| system     | service station        |                   |                  |               |         |                        |                                               |
|                        | Nervous       | attendant               |                   |                  |               |         |                        |                                               |
|                        | Nervous       | Machinist, miner,      |                   |                  |               |         |                        |                                               |
|                        | system       | lumberman              |                   |                  |               |         |                        |                                               |
| Hakulinen et al., 1976 (19)| Brain   | Motor vehicle           |                   |                  |               |         |                        |                                               |
|                        |              | mechanics,             |                   |                  |               |         |                        |                                               |
|                        |              | machinists, miners,    |                   |                  |               |         |                        |                                               |
|                        |              | painters, dyers,       |                   |                  |               |         |                        |                                               |
|                        |              | printers               |                   |                  |               |         |                        |                                               |
|                        |              | motor vehicle drivers  |                   |                  |               |         |                        |                                               |
|                        |              | motor vehicle          |                   |                  |               |         |                        |                                               |
|                        | Paint        | At birth               | [2.82]            | S                | 10            |         |                        |                                               |
| Hydrocarbons           | Nervous       | Machinist, miner,      |                   |                  |               |         |                        |                                               |
|                        | system       | lumberman              |                   |                  |               |         |                        |                                               |
| Hakulinen et al., 1976 (19)| Brain   | Motor vehicle           |                   |                  |               |         |                        |                                               |
|                        |              | mechanics,             |                   |                  |               |         |                        |                                               |
|                        |              | machinists, miners,    |                   |                  |               |         |                        |                                               |
|                        |              | painters, dyers,       |                   |                  |               |         |                        |                                               |
|                        |              | printers               |                   |                  |               |         |                        |                                               |
|                        |              | motor vehicle          |                   |                  |               |         |                        |                                               |
|                        | Paint        | After birth            | Infinity          | 0.7–infinity     | 4*            |         |                        |                                               |

(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      | Mechanics, service station attendants                      | HCs      | At birth       | 1.00          | NS     | 6                      |          |
|                            | system       | Machinists                                                | HCs      |                | 0.70          | NS     | 9                      |          |
|                            |              | Miners, engineering and allied trades, textiles, printing press operators, painters and decorators, dry cleaners, motor vehicle drivers | HCs | | | | | |
| Sanders at al., 1981 (4)   | Brain        | Factory workers, machinists, drivers, motor vehicle mechanics, service station attendants, lumbermen, painters, dyers, cleaners | HCs      | Before birth   | 0.54–2.3      | NS     | 10–20*                 | Results are for two control groups |
| Gold et al., 1982 (18)     | Brain        | Factory workers, machinists, drivers, motor vehicle mechanics, service station attendants, lumbermen, painters, dyers, cleaners | HCs      | After birth    | 0.85          | NS     | 24*                   | Healthy controls |
|                            |              | Aromatic and aliphatic HCs                                |          |                | 4.00          | S      | 15#                   | Cancer controls |
| Spitz and Johnson, 1985 (6) | Neuroblastoma | HCs                                                      |          | At birth       | NA            | NS     | NA                    |          |
| Johnson et al., 1987 (13)  | Nervous      | Aircraft industry workers                                  | HCs      | At birth       | 0.7–1.1       | NS     | NA                    | Results are for different groups of HC-related jobs |
|                            | system       | Machine repairmen                                          | HCs      |                | 1.00          | 0.5–2.3 | NA                    |          |
|                            |              | Paper and pulp mill workers                                | HCs      |                | 1.50          | 0.8–2.7 | NA                    |          |
|                            |              | Factory workers, machinists, steelworkers                  | HCs      |                | 4.00          | 0.4–43.7 | NA                    |          |
|                            |              | Motor vehicle mechanics, machinists, miners, painters, dyers, printers | HCs      |                | 1.20          | 0.9–1.6 | NA                    |          |
|                            |              | Motor vehicle mechanics, service station attendants        | HCs      |                | 1.00          | 0.7–1.6 | NA                    |          |
| Nasca et al., 1988 (21)    | CNS          | Narrow definition                                          | HCs      | At birth       | 1.25          | 0.7–2.4 | 18                    |          |
|                            |              | Broad definition                                           | HCs      | At diagnosis   | 1.11          | 0.5–2.3 | 13                    |          |
|                            |              |                                                            | HCs      | At birth       | 1.41          | 0.9–2.2 | 38                    |          |
|                            |              |                                                            | HCs      | 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                     |          |
|                            |              | Alkylation agents                                          |          |                | 1.30          | 0.4–4.0 | 9                     |          |
|                            |              | Aliphatic HCs                                             |          |                | 0.90          | 0.3–2.2 | 15                    |          |
| Metals                    | Brain        | Metal industry                                            | HCs      | At birth       | 1.80          | 1.1–2.9 | 62                    |          |
| Wilkins and Koutras, 1988 (7) |          | Metal related occupations                                 | HCs      |                | 1.60          | 1.1–2.3 | 93                    |          |
|                            |              | Metal industry: processing occupations                     | HCs      |                | 5.30          | 1.0–27.2 | 9                     |          |
|                            |              | Metal industry: machine trades occupations                | HCs      |                | 1.40          | 0.6–3.2 | 17                    |          |
|                            |              | Metal industry: structural work occupations               | HCs      |                | 3.90          | 1.2–12.8 | 12                    |          |
|                            |              | Machine trades occupations: metal machining occupations | HCs      |                | 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 | 41a | |
| | | | During pregnancy | | 0.90 | 0.4-2.0 | 32a | |
| | | | After birth | | 0.80 | 0.4-1.8 | 33a | |
| 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., 1978 (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
  - HCs
  - After birth
  - 0.60
  - NS
  - 5
- Hemminki et al., 1981 (12)
  - Brain
  - Motor vehicle driver
  - HCs
  - During pregnancy
  - 0.92
  - NS
  - 84a
- Gold et al., 1982 (18)
  - Brain
  - Driver, mechanic, service station attendant, railroad worker/engineer
  - HCs
  - Before birth
  - 0.33-0.50
  - NS
  - 6-12a
- 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
  - HCs
  - At birth
  - 1.60
  - 1.0-2.4
  - 97
- Howe et al., 1989 (24)
  - Brain
  - Drivers
  - HCs
  - Before birth
  - 3.70
  - 0.7-20.7
  - 5
- Wilkins and Sinks, 1990 (16)
  - Brain
  - Motor freight and transportation
  - HCs
  - Preconception
  - 2.30
  - 0.7-8.1
  - 6
- Wilkins and Hundley, 1990 (25)
  - Neuroblastoma
  - Transportation industry: motor freight and transportation
  - HCs
  - At birth
  - 0.80
  - 0.4-1.5
  - 18

(Continued)
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)). Buckely 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 parental 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 (41,18–20,22,28,31,41). 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

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### 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 | Transportation industry | Preconception | 0.50 | 0.2–1.3 | 21* |          |
| | | | During pregnancy | 0.10 | 0.0–0.6 | 16* |          |
| | | | After birth | 0.60 | 0.2–1.4 | 30* |          |
| | | | Motor vehicle | Preconception | 0.90 | 0.4–2.0 | 32* |          |
| | | | exhausts, more | During pregnancy | 0.70 | 0.2–2.6 | 12* |          |
| | | | Motor vehicle | After birth | 1.00 | 0.6–78.4 | 2* |          |
| | | | exhausts, less | During pregnancy | 0.50 | 0.2–1.3 | 23* |          |
| | | | exposure | After birth | 0.70 | 0.3–1.7 | 27* |          |

Abbreviations: S, significant; NS, not significant; NA, not available from published report. *number of discordant pairs. [1], calculated by the authors of this review.
Table 3. Childhood leukemia and paternal occupations with significant findings in multiple studies.

| Reference                | 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 (29)| 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 (29)| 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 (29)| Acute leukemia        | Toluene  | Year before conception to reference date | NA          | NS      | NA                      |          |
|                          |                        |          | Year before pregnancy | 1.70      | NS      | 8a                      | Significant trend with frequency of use (p=0.03). |
|                          |                        |          | After birth      | 1.70          | NS      | 8a                      |          |
|                          |                        |          | During pregnancy | 3.00          | 0.8-17.2 | 12a                     |          |
| Chlorinated solvents     |                        |          | Year before pregnancy | 2.20      | NS      | 13a                     | Significant trend with frequency of use (p=0.03). OR retains significance after adjusting for other exposures. |
|                          |                        |          | After birth      | 3.50          | 1.1-14.6 | 18a                     |          |
| Carbon tetrachloride     |                        |          | Year before pregnancy | 0.70      | NS      | 5a                      | Not independent of observation for benzene, wood, and radiation. |
|                          |                        |          | During pregnancy | 0.70          | NS      | 5a                      |          |
|                          |                        |          | After birth      | 1.70          | 0.3-10.7 | 8a                      |          |
| McKinney et al., 1991 (29)| Leukemia + NHL        | Carbon tetrachloride | Preconception    | 2.90          | 1.1-7.4  | 13                     |          |
|                          |                        |          | During pregnancy | 2.16          | 0.5-9.1  | 5                       |          |
|                          |                        |          | After birth      | 3.48          | 0.5-17.2 | 6                       |          |
| Lowengart et al., 1987 (29)| Acute leukemia        | TCE      | Year before pregnancy | 2.00      | NS      | 9a                      |          |
|                          |                        |          | During pregnancy | 2.00          | NS      | 9a                      |          |
|                          |                        |          | After birth      | 2.70          | 0.6-15.6 | 11a                     |          |

(Continued)
| Reference                  | Histology          | Industry or occupation | Exposure | Time frame     | Relative risk | 95% CI   | Number of exposed cases | Comments                                                                 |
|----------------------------|--------------------|------------------------|----------|----------------|---------------|----------|------------------------|---------------------------------------------------------------------------|
| McKinney et al., 1991 [29] | Leukemia           | Painters               | TCE      | Preconception  | 2.27          | 0.8–6.2  | 9                      | OR calculated by Savitz and Chen (1990) (2).                               |
|                            |                   |                        |          |                |               |          |                        |                                                                           |
| Lowengart et al., 1987 [26]| Acute leukemia     | Painters               | PCE      | After birth    | 2.66          | 0.8–9.2  | 7                      |                                                                           |
| Paints and pigments        | Leukemia           | Painters               | HCs      | At birth       | 0.90          | NS       | 7                      |                                                                           |
| Kwa and Fine, 1980 [20]    | Leukemia + lymphoma| Painters               | HCs      | At birth       | 0.90          | NS       | 7                      |                                                                           |
| Hemminki et al., 1981 [12] | Leukemia           | Painters               | HCs      | At birth       | 0.90          | NS       | 7                      |                                                                           |
| Van Steensel-Moll et al., 1985 [31] | ALL | Painters               | Painters | At birth       | 0.90          | NS       | 7                      |                                                                           |
| Lowengart et al., 1987 [26]| Acute leukemia     | Painter                | HCs      | At birth       | 0.90          | NS       | 7                      |                                                                           |
| Buckley et al., 1989 [27]  | ANLL               | Painters               | Ever     | 7.00           | S             | 7        |                        |                                                                           |
| McKinney et al., 1991 [29] | Leukemia + NHL     | Painters               | Ever     | 7.00           | S             | 7        |                        |                                                                           |
| Motor vehicle-related occupations | Leukemia + lymphoma | Painters | Painters | Ever | 7.00 | S | 7 | Authors say “failed to confirm association.” |
| Fabia and Thuy, 1974 [17]  | Leukemia           | Motor vehicle mechanic, service station attendant | HCs | At birth | [2.03] | S | 16 | ORs calculated by Savitz and Chen (1990) (2). |
| Hakulinen et al., 1976 [19] | Leukemia           | Motor vehicle drivers  | HCs | During pregnancy | 1.06 | 0.6–1.8 | [35] | Results are for entire study period. |
| Kwa and Fine, 1980 [20]    | Leukemia + lymphoma| Mechanics, gas station attendants | HCs | At birth | 1.10 | NS | 21 | Results are for 1969–1975 only. |
| Hemminki et al., 1981 [12] | Leukemia           | Motor vehicle drivers  | HCs | During pregnancy | 1.10 | NS | 21 | Results are for healthy controls. |
| Gold et al., 1982 [18]     | Leukemia           | Motor vehicle related (driver, mechanic, service station attendant, railroad worker/engineer) | HCs | Before birth | 0.75 | NS | 7 | 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 | 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.,             | Acute leukemia     |                        | Moderate: cab driver,|                    | 2.50          | S      | 28*                     | Results are for control group A.             |
| 1984 (33)                  |                    |                        | traveling salesman,  |                    |               |        |                         |                                               |
|                            |                    |                        | truck or bus driver, |                    |               |        |                         |                                               |
|                            |                    |                        | railroad worker,     |                    |               |        |                         |                                               |
|                            |                    |                        | toll booth attendant,|                    |               |        |                         |                                               |
|                            |                    |                        | highway worker,      |                    |               |        |                         |                                               |
|                            |                    |                        | police officer       |                    |               |        |                         |                                               |
|                            |                    |                        | Motor vehicle        | Before birth       | 1.27          | NS     | 25*                     | Results are for control group B.             |
|                            |                    |                        | exhaust              |                    |               |        |                         |                                               |
| Van Steensel-Moll et al., | ALL                | Exhaust gases          |                      | During pregnancy   | 3.75          | S      | 19*                     | Results are for control group B.             |
| 1985 (31)                  |                    |                        |                      |                    |               |        |                         |                                               |
| Shu et al.,                | Leukemia           | Transportation         |                      | During pregnancy   | 1.30          | 0.8–1.9| 89                      |                                               |
| 1988 (43)                  |                    | equipment operator     |                      |                    |               |        |                         |                                               |
| Buckley et al.,            | ANLL               | Nonauto mechanics      |                      | Ever               | 3.50          | S      | 14                      |                                               |
| 1989 (27)                  |                    |                        |                      |                    |               |        |                         |                                               |
| Magnani et al.,            | NHL                | Lorry driver           |                      | Before birth       | 5.00          | 1.1–22.4| 2                       |                                               |
| 1990 (32)                  |                    |                        |                      | After birth        | 5.00          | 1.1–22.4| 2                       |                                               |
| McKinney et al.,           | Leukemia           | Exhaust fumes          |                      |                    | NA            | NS     | NA                      |                                               |
| 1991 (29)                  |                    |                        |                      |                    |               |        |                         |                                               |
| Roman et al.,              | Leukemia           | Drivers and related    |                      | At birth           | 0.60          | 0.1–2.0| 3                       | Range of ORs for different control groups and exposure intensities. |
| 1993 (36)                  |                    |                        |                      | Before birth       | 1.30          | 0.4–3.2| 7                       | Range of ORs for different control groups and exposure intensities. |
|                            |                    |                        |                      |                    |               |        |                         |                                               |
| Ionizing radiation         |                    |                        |                      |                    |               |        |                         |                                               |
| Hicks et al.,              | Leukemia           | Occupations            | Ionizing radiation  | Year before birth  | 0.78–1.41     | NS     | 10–27                   | Range of ORs for different control groups and exposure intensities. |
| 1984 (34)                  |                    |                        |                      |                    |               |        |                         |                                               |
|                            |                    |                        | 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.,  | Leukemia           | Radioactivity          |                      | During pregnancy   | 1.40          | 0.6–3.5| 13                      | Area controls.                                |
| 1985 (31)                  |                    |                        |                      |                    |               |        |                         |                                               |
| Buckley et al.,            | Leukemia           | Ionizing radiation     |                      | Ever               | 1.90          | NS     | 17                      | Local controls.                               |
| 1989 (27)                  |                    |                        |                      |                    |               |        |                         |                                               |
| Gardner et al.,            | Leukemia           | Nuclear plant          | External ionizing   | Preconception      | 8.38          | 1.4–52.0| 4                       | For external radiation doses exceeding 100 mSv. Area controls. For external radiation doses exceeding 100 mSv. Local controls. |
| 1990 (35)                  |                    |                        | radiation            |                    |               |        |                         |                                               |
|                            |                    |                        |                      |                    |               |        |                         |                                               |
| Urrhart et al.,            | Leukemia           | Nuclear industry       | Radiation            | At conception      | 0.58          | 0.1–2.6| 3                       | Study population overlaps with Gardner et al. (1990) (35). |
| 1991 (37)                  |                    |                        |                      |                    |               |        |                         |                                               |
| McKinney et al.,           | Leukemia           | Radiation              | Preconception        | 3.23               | 1.4–7.7      | 15      | 8                       | Study population overlaps with Gardner et al. (1990) (35). |
| 1991 (29)                  |                    |                        |                      |                    |               |        |                         |                                               |
| Kinlen et al.,             | Leukemia           | Nuclear industry       | Ionizing radiation  | Preconception      | 1.26          | 0.6–3.9| 11                      |                                               |
| 1993 (36)                  |                    |                        |                      |                    |               |        |                         |                                               |
| Roman et al.,              | Leukemia           | Nuclear industry       | Ever                 | 2.50               | 0.6–9.0     | 4       | 4                       |                                               |
| 1993 (36)                  |                    |                        | Preconception        | 2.80               | 0.6–10.5    | 4       | 4                       |                                               |
|                            |                    |                        | Ever                 | 8.00               | 1.4–54.6    | 4       | 4                       |                                               |
|                            |                    |                        |                      |                    |               |        |                         |                                               |
| Mclaughlin et al.,         | Leukemia           | Nuclear industry       | External ionizing    | Preconception      | 1.45          | 0.8–2.8| 29                      |                                               |
| 1981 (39)                  |                    |                        | radiation            |                    |               |        |                         |                                               |
| Sorahan et al.,            | Leukemia           | (predominantly)        | External ionizing    | Preconception      | 2.75          | 0.9–8.6| 11                      |                                               |
| 1993 (40)                  |                    |                        | radiation            |                    |               |        |                         |                                               |

NA, Not available from published report; S, significant; NS, not significant. *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) 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 mechansitic 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.

### 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 | |          |
| Lowengart et al., 1987 (29) | 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 | |          |
| McKinney et al., 1991 (29) | Leukemia + NHL | Catering, cleaning, hairdressing | Preconception | 2.94 | 1.6–5.2 | 38 | |          |
| 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 | |          |
| 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                |           |                        |          |                     | 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 | |          |
|                         | Metal dusts | During pregnancy | 3.00 | NS | NA | |          |
|                         | Metal dusts | 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 benz[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 village. 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.,  | 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                      |          |
| 1979 (46)       |           | Machinist, cleaner, embalmer Driver, motor vehicle mechanic, service station attendant  | HCs only |            | 1.40          |        | 7                       |          |
|                 |           |                                                                                        | HCs only |            | 3.40          |        | 17                      |          |
| Kwa and Fine,   | Wilms     | Mechanics, gas station attendants, machinists                                        | HCs      |            | 2.50          | S      | 10                      |          |
| 1980 (20)       |           |                                                                                        |          |            |               |        |                         |          |
| Sanders et al., | Wilms     | Miners, engineering and allied trades, textile workers, printers, painters, decorators, | HCs      | At child’s death | 1.19          |        | 79                      |          |
| 1981 (4)        |           | dry cleaners, motor vehicle drivers                                                   |          |            |               |        |                         |          |
| Wilkins and Sinks, | Wilms | Motor vehicle mechanic, service station attendant, driver/heavy equipment operator, | HCs      | At birth  | 1.4           | 0.7–2.7 | 19                      |          |
| 1984 (47)       |           | metal worker/machinist, lumberman, miner, painter, printer, leather worker, factory worker |          |            |               |        |                         |          |
| Bunin et al.,   | Wilms     | HCs                                                                                    |          | Age 18–after birth | NA          |        | NA                      |          |
| 1989 (44)       |           |                                                                                        |          |            |               |        |                         |          |

The authors conclude that increased risk is due to lead rather than HCs.
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 is uncertain whether the type of parental exposure and 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 preconception (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 childhood 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.

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