

# **Toxic chemicals and childhood cancer: A review of the evidence**

Tami Gouveia-Vigeant, MPH, MSW and Joel Tickner, ScD

With contributions from Richard Clapp, DSc<sup>1</sup>

May, 2003

A Publication of the Lowell Center for Sustainable Production

University of Massachusetts Lowell  
One University Avenue  
Lowell, MA 01854  
978-934-2981  
[sustainableproduction.org](http://sustainableproduction.org)

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<sup>1</sup> Department of Environmental Health, Boston University School of Public Health

## **EXECUTIVE SUMMARY**

Childhood cancer is the second largest cause of death to children ages 0-15 in the United States (second only to accidents), and more than 8,000 cases are diagnosed each year. In Massachusetts from 1990-1999, approximately 2,688 children ages 0-19 were diagnosed with cancer and 394 died. The overall rate of childhood cancer in Massachusetts is slightly higher than the national average—16.7 new cases versus 16.1 per 100,000 per year. African American and Latino children in Massachusetts had approximately 25% more diagnosed cancers than white and Asian and Pacific Islander children.

Although childhood cancer is a relatively rare disease, cancer rates increased nearly 21% between 1975 and 1998—approximately 1% each year. Some causes of cancer can be attributed to genetic predisposition, while it is highly likely that environmental exposures, including toxic substances in our environment, food, water, and consumer products, play a role. A panel of experts convened by Mt. Sinai Hospital recently concluded that genetic predisposition accounts for no more than 20% of all childhood cancers and that the environmental attributable fraction of childhood cancer could be between 5% and 90%, depending on the type of cancer. This means that a potentially large percentage of childhood cancers is preventable.

There are some well-established links between environmental exposures and childhood cancer, including: pharmaceuticals such as diethylstilbestrol (DES), an estrogen prescribed from the late 1940s to the early 1970s to prevent miscarriage; ionizing radiation; and chemotherapeutic agents. However, evidence increasingly indicates that parental and childhood exposures to certain toxic chemicals including solvents, pesticides, petrochemicals and certain industrial by-products (dioxins and polycyclic aromatic hydrocarbons) can result in childhood cancer.

This report, commissioned by the Massachusetts Alliance for a Healthy Tomorrow, examines the evidence linking exposures to solvents, pesticides, petrochemicals, and certain industrial by-products with cancer in children. The report is based on examination of the published literature

on epidemiologic studies, animal toxicologic data, reviews of published studies and analyses of studies, case reports, fact sheets, and conference summaries.

Our analysis found the following:

- Epidemiologic studies have consistently found an increased likelihood of certain types of childhood cancer following parental and childhood exposure to pesticides and solvents.

Studies indicate that parental exposure to certain petroleum-based chemicals and parental and childhood exposure to combustion by-products, such as dioxins and polycyclic aromatic hydrocarbons, may increase the likelihood of childhood leukemia and brain and central nervous system cancers.

In one study of pesticide exposures, children with leukemia were 4 to 7 times as likely to have been exposed to pesticides used in the yard or garden compared to children without the disease. Another study found that children with leukemia were 11 times as likely to have mothers who were exposed to pesticide sprays or foggers during pregnancy compared to healthy children. Compared to children of unexposed fathers, children whose fathers were occupationally exposed to benzene and alcohols used in industrial products were nearly 6 times as likely to develop leukemia if the exposure occurred prior to the pregnancy. In Dover Township, New Jersey, researchers found that children with leukemia were 5.4 times as likely as children without leukemia to have drunk water from private wells in groundwater areas with a history of contamination from the Reich Farm Superfund site or wastewater from a nearby industrial facility. In another study, children with acute non-lymphocytic leukemia (ANLL) were 2.4 times as likely as those without ANLL to have parents who were exposed to petroleum products in their jobs.

This evidence is supported by laboratory experiments and data on adult cancers from similar exposures. In most cases, the studies do not provide evidence of cancer from exposure to particular chemicals but rather mixtures or classes of chemicals (e.g., pesticides, solvents, hydrocarbons).

- Exposures that occur prior to conception, in the womb, and in early childhood can increase the likelihood of childhood cancer. Cancer may develop in the fetus if the germ cells (sperm and eggs) of the mother or father are damaged prior to pregnancy. Also, a fetus may be exposed to potentially harmful chemicals *in utero*. In such cases, the toxic substance can cross the placenta and enter the body of a developing fetus, potentially leading to cancer.

Based on the literature, the types of exposures that have the strongest apparent links to childhood cancer include: parental exposure to pesticides from occupational, agricultural, home, and garden uses; parental exposure to solvents in manufacturing and painting; parental occupational exposure to hydrocarbons; maternal exposure to water contaminated with solvents; direct childhood exposure to pesticides from home and garden use; childhood exposure to solvents in drinking water; and childhood exposure to dioxins.

- The evidence supporting the connection between exposure to these toxicants and childhood cancer is strongest for leukemia, brain and central nervous system cancers.

It is difficult to determine the exact magnitude of the contribution of toxic chemicals to the overall burden of childhood cancer. Because the majority of chemicals in commerce—some of which are widely used in everyday products—have not been studied for their potential to cause cancer, we do not have a complete picture of the potential chemical causes of cancer in children. The links with childhood cancer have been adequately studied for only a few chemicals. Mixtures of chemicals mimicking the complex exposures that occur in everyday life have been studied even less.

Since people are exposed to many chemicals and other agents simultaneously, and cancer is a rare disease, it is very difficult to establish causal links. Because of these difficulties and the costs of studies, relatively few epidemiologic studies examining the links have been conducted. Further, many studies that have been conducted have serious limitations and could be expected

to provide only weak evidence about causes and childhood cancer. The lack of proof of direct causal links between toxics and childhood cancer should not be construed as proof of safety. There are far more chemicals in circulation with little or no evidence of harm or safety than there are chemicals tested regularly and shown to be safe.

The evidence presented in this report indicates that preventing parental and childhood exposure to chemicals suspected of causing cancer can have important health benefits. The types of chemicals examined in this report are of concern not only for their ability to cause cancer but other health effects as well—neurological and developmental harms to the fetus, for example. Preventing exposure to chemicals suspected of causing cancer is possible, as recent European policies demonstrate. The European Union will soon require that all chemicals in commercial circulation receive basic testing, and that those that are known or probable carcinogens, mutagens, or reproductive toxicants be used only when there are no safer economically and technically feasible alternatives. This common sense approach to chemical safety is likely to result in significant reductions in childhood exposure to potentially dangerous chemicals.

**Table 1. Evidence of links between toxic chemical exposures and childhood leukemia**

| <b>Cancer or Tumor Type</b> | <b>Toxic Exposure</b>   | <b>Source of Exposure</b>                            | <b>Timing or Duration</b>                            | <b>Reference</b>                |
|-----------------------------|---|--|--|---------------------------------|
| Leukemia                    | <ul style="list-style-type: none"> <li>• Professional pest control services</li> </ul>                        | Residential exposures to fetus and children          | 1 year before and 3 years after birth                | Ma, et al., 2002                |
|                             | <ul style="list-style-type: none"> <li>• Pest strips</li> </ul>   | Residential exposures to mothers                     | During pregnancy                                     | Leiss and Savitz, 1995          |
|                             | <ul style="list-style-type: none"> <li>• Pesticides</li> </ul>  | Residential (farm) exposures to parents and children | Childhood  | Lowengart, et al., 1987         |
|                             | <ul style="list-style-type: none"> <li>• Trichloroethylene</li> <li>• Tetrachloroethylene</li> </ul>          | Environmental exposures to children                  | Childhood  | Fagliano, et al., 2003          |
|                             | <ul style="list-style-type: none"> <li>• Trichloroethylene</li> <li>• Tetrachloroethylene</li> </ul>          | Environmental exposures to mothers                   | During pregnancy                                     | Fagliano, et al., 2003          |
|                             | <ul style="list-style-type: none"> <li>• Solvent mixture including Trichloroethylene</li> </ul>               | Environmental exposures to mothers                   | During pregnancy                                     | Costas, et al., 2002            |
|                             | <ul style="list-style-type: none"> <li>• Benzene</li> <li>• Perchloroethylene</li> </ul>                      | Environmental (air) exposures                        | Not given  | Reynolds, et al., 2002b         |
|                             | <ul style="list-style-type: none"> <li>• Solvents</li> </ul>  | Occupational exposures to fathers                    | Prior to pregnancy                                   | Feychting, et al., 2001         |
|                             | <ul style="list-style-type: none"> <li>• Benzene</li> <li>• Alcohols</li> </ul>                               | Occupational exposures to fathers                    | Prior to pregnancy                                   | McKinney, et al., 1991          |
|                             | <ul style="list-style-type: none"> <li>• Chlorinated solvents</li> <li>• Methyl ethyl ketone (MEK)</li> </ul> | Occupational exposures to fathers                    | Before and during pregnancy and after birth of child | Lowengart, et al., 1987         |
| Leukemia                    | <ul style="list-style-type: none"> <li>• Diesel exhaust and PAHs</li> </ul>                                   | Environmental (air) exposures to children            | Childhood  | Lagorio, et al., 2000           |
|                             | <ul style="list-style-type: none"> <li>• Motor vehicle exhaust (nitrogen dioxide)</li> </ul>                  | Occupational exposures to fathers                    | Before pregnancy                                     | Feychting, et al., 1998         |
|                             | <ul style="list-style-type: none"> <li>• Dioxin</li> </ul>  | Environmental (air) exposures to children            | Childhood  | Bertazzi, et al., 1992          |
|                             | <ul style="list-style-type: none"> <li>• Hydrocarbon-related occupations</li> </ul>                           | Occupational exposures to women                      | During pregnancy                                     | van Steensel-Moll, et al., 1985 |

**Table 2. Evidence of links between toxic chemical exposures and childhood leukemia (specific cell types)**

| <b>Cancer or Tumor Type</b>           | <b>Toxic Exposure</b>  | <b>Source of Exposure</b>           | <b>Timing or Duration</b>                            | <b>Reference</b>             |
|---------------------------------------|--|-------------------------------------|--|------------------------------|
| Acute Lymphocytic Leukemia (ALL)      | <ul style="list-style-type: none"> <li>• Pest strips</li> <li>• Insecticides/rodenticides</li> <li>• Garden herbicides and products for tree infestations</li> </ul> | Residential exposures to mothers    | During pregnancy                                     | Infante-Rivard, et al., 1999 |
|                                       | <ul style="list-style-type: none"> <li>• Pesticides</li> </ul>   | Occupational exposures to mothers   | During pregnancy                                     | Shu, et al., 1988            |
|                                       | <ul style="list-style-type: none"> <li>• Trichloroethylene</li> <li>• Carbon tetrachloride</li> <li>• Perchloroethylene</li> </ul>                                   | Occupational exposures to mothers   | Before and during pregnancy and after birth of child | Shu, et al., 1999            |
|                                       | <ul style="list-style-type: none"> <li>• Trichloroethylene</li> <li>• Carbon tetrachloride</li> <li>• Perchloroethylene</li> </ul>                                   | Environmental exposures to children | Childhood  | Shu, et al., 1999            |
|                                       | <ul style="list-style-type: none"> <li>• Exhaust</li> </ul>  | Occupational exposures to mothers   | Before pregnancy                                     | Shu, et al., 1999            |
|                                       | <ul style="list-style-type: none"> <li>• PAHs</li> <li>• Gasoline</li> </ul>   | Occupational exposures to mothers   | Before and during pregnancy                          | Shu, et al., 1999            |
| Acute Non-Lymphocytic Leukemia (ANLL) | <ul style="list-style-type: none"> <li>• Pesticides</li> </ul>   | Residential exposures to mothers    | During pregnancy                                     | Buckley, et al., 1989        |
|                                       | <ul style="list-style-type: none"> <li>• Pesticides</li> </ul>   | Occupational exposures to fathers   | Jobs held more than 1,000 days                       | Buckley, et al., 1989        |
|                                       | <ul style="list-style-type: none"> <li>• Pesticides</li> </ul>   | Residential exposures to children   | Childhood  | Buckley, et al., 1989        |
|                                       | <ul style="list-style-type: none"> <li>• Solvents</li> </ul>   | Occupational exposures to fathers   | Not given  | Buckley, et al., 1989        |
|                                       | <ul style="list-style-type: none"> <li>• Benzene</li> </ul>  | Occupational exposures to mothers   | During pregnancy                                     | Shu, et al., 1988            |
|                                       | <ul style="list-style-type: none"> <li>• Petroleum products</li> <li>• Gasoline</li> </ul>   | Occupational exposures to fathers   | Not given  | Buckley, et al., 1989        |
|                                       |  | Occupational exposures to mothers   | During pregnancy                                     | Shu, et al., 1988            |



**Table 3. Evidence of links between toxic chemical exposures and childhood brain and CNS cancer**

| <b>Cancer or Tumor Type</b> | <b>Toxic Exposure</b>  | <b>Source of Exposure</b>                            | <b>Timing or Duration</b> | <b>Reference</b>                |
|-----------------------------|--|--|---------------------------|---------------------------------|
| Nervous System Tumor        | • Pesticides   | Occupational (farm or forestry) exposures to fathers | Near conception           | Feychting, et al., 2001         |
|                             | • Solvents   | Occupational exposures to fathers                    | Near conception           | Feychting, et al., 2001         |
|                             | • Motor vehicle exhaust (nitrogen dioxide)                               | Environmental (air) exposures to children            | Childhood                 | Feychting, et al., 1998         |
| Brain Tumor                 | • Insecticides, including flea and tick products<br>• Sprays and foggers | Residential exposures to mothers                     | During pregnancy          | Pagoda and Preston-Martin, 1997 |
|                             | • Horticultural and pesticide indicators                                 | Occupational (farm) exposures to parents             | Not given                 | Kristensen, et al., 1996        |
|                             | • Pesticides   | Residential (farm) exposures to mothers              | During pregnancy          | Bunin, et al., 1994             |
|                             | • Pesticides   | Residential (farm) exposures                         | Not given                 | Cordier, et al., 1994           |
|                             | • Pest strips<br>• Flea collars<br>• Herbicides/Insecticides             | Residential exposures to children                    | Childhood                 | Davis, et al., 1993             |
| Neuroblastoma               | • Pesticides   | Residential exposures to children                    | Not given                 | Daniels, et al., 2001           |
|                             | • Horticultural and pesticide indicators                                 | Occupational (farm) exposures to parents             | Not given                 | Kristensen, et al., 1996        |
|                             | • Benzene<br>• Alcohols<br>• Lacquer thinner<br>• Turpentine             | Occupational exposures to fathers                    | Not given                 | De Roos, et al., 2001           |
|                             | • Hydrocarbons, including diesel fuel                                    | Occupational exposures to fathers                    | Not given                 | De Roos, et al., 2001           |
|                             | • Aromatic hydrocarbons<br>• Aliphatic hydrocarbons                      | Occupational exposures to parents                    | Not given                 | Spitz and Johnson, 1985         |

**Table 4. Evidence of links between toxic chemical exposures and other childhood cancers**

| <b>Cancer or Tumor Type</b>  | <b>Toxic Exposure</b>                                | <b>Source of Exposure</b>                | <b>Timing or Duration</b> | <b>Reference</b>         |
|------------------------------|--|--|---------------------------|--------------------------|
| Non-Hodgkin's Lymphoma (NHL) | • Insecticides, including professional extermination | Residential exposures to children        | Childhood                 | Meinert, et al., 2000    |
|                              | • Horticultural and pesticide indicators             | Occupational (farm) exposures to parents | Not given                 | Kristensen, et al., 1996 |
| Soft tissue sarcoma (STS)    | • Yard pesticides                                    | Residential exposures to children        | Childhood                 | Leiss and Savitz, 1995   |
| Hepatoblastoma               | • Hydrocarbons                                       | Occupational exposures to mothers        | Not given                 | Robison, et al., 1995    |
|                              | • Petroleum products                                 | Occupational exposures to fathers        | Not given                 | Robison, et al., 1995    |
| Wilms' tumor                 | • Pesticides   | Occupational (farm) exposures to parents | Not given                 | Kristensen, et al., 1996 |
|                              | • Pesticides   | Occupational (farm) exposures to parents | Not given                 | Sharpe, et al., 1995     |
|                              | • Pesticides   | Residential exposures                    | Not given                 | Olshan, et al., 1993     |
|                              | • Hydrocarbons                                       | Occupational exposures to parents        | Not given                 | Colt and Blair, 1998     |
|                              | • Hydrocarbons                                       | Occupational exposures to parents        | Not given                 | Wilkins and Sinks, 1984  |
| Urinary tract cancer         | • Hydrocarbons                                       | Occupational exposures to parents        | Not given                 | Kwa and Fine, 1980       |