Toxic chemicals and childhood cancer: A review of the evidence

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May, 2003

A Publication of the Lowell Center for Sustainable Production

University of Massachusetts Lowell
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Lowell, MA 01854
978-934-2981
sustainableproduction.org

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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

Cancer or Tumor Type	Toxic Exposure	Source of Exposure	Timing or Duration	Reference
Leukemia	• Professional pest control services	Residential exposures to fetus and children	1 year before and 3 years after birth	Ma, et al., 2002
	• Pest strips	Residential exposures to mothers	During pregnancy	Leiss and Savitz, 1995
	• Pesticides	Residential (farm) exposures to parents and children	Childhood	Lowengart, et al., 1987
	• Trichloroethylene • Tetrachloroethylene	Environmental exposures to children	Childhood	Fagliano, et al., 2003
	• Trichloroethylene • Tetrachloroethylene	Environmental exposures to mothers	During pregnancy	Fagliano, et al., 2003
	• Solvent mixture including Trichloroethylene	Environmental exposures to mothers	During pregnancy	Costas, et al., 2002
	• Benzene • Perchloroethylene	Environmental (air) exposures	Not given	Reynolds, et al., 2002b
	• Solvents	Occupational exposures to fathers	Prior to pregnancy	Feychting, et al., 2001
	• Benzene • Alcohols	Occupational exposures to fathers	Prior to pregnancy	McKinney, et al., 1991
	• Chlorinated solvents • Methyl ethyl ketone (MEK)	Occupational exposures to fathers	Before and during pregnancy and after birth of child	Lowengart, et al., 1987
	• Diesel exhaust and PAHs	Environmental (air) exposures to children	Childhood	Lagorio, et al., 2000
	• Motor vehicle exhaust (nitrogen dioxide)	Occupational exposures to fathers	Before pregnancy	Feychting, et al., 1998
	• Dioxin	Environmental (air) exposures to children	Childhood	Bertazzi, et al., 1992
	• Hydrocarbon-related occupations	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)

Cancer or Tumor Type	Toxic Exposure	Source of Exposure	Timing or Duration	Reference
Acute Lymphocytic Leukemia (ALL)	• Pest strips • Insecticides/rodenticides • Garden herbicides and products for tree infestations	Residential exposures to mothers	During pregnancy	Infante-Rivard, et al., 1999
	• Pesticides	Occupational exposures to mothers	During pregnancy	Shu, et al., 1988
	• Trichloroethylene • Carbon tetrachloride • Perchloroethylene	Occupational exposures to mothers	Before and during pregnancy and after birth of child	Shu, et al., 1999
	• Trichloroethylene • Carbon tetrachloride • Perchloroethylene	Environmental exposures to children	Childhood	Shu, et al., 1999
	• Exhaust	Occupational exposures to mothers	Before pregnancy	Shu, et al., 1999
	• PAHs	Occupational exposures to mothers	Before and during pregnancy	Shu, et al., 1999
	• Gasoline	Occupational exposures to mothers	During pregnancy	Shu, et al., 1988
Acute Non-Lymphocytic Leukemia (ANLL)	• Pesticides	Residential exposures to mothers	During pregnancy	Buckley, et al., 1989
	• Pesticides	Occupational exposures to fathers	Jobs held more than 1,000 days	Buckley, et al., 1989
	• Pesticides	Residential exposures to children	Childhood	Buckley, et al., 1989
	• Solvents	Occupational exposures to fathers	Not given	Buckley, et al., 1989
	• Benzene	Occupational exposures to mothers	During pregnancy	Shu, et al., 1988
	• Petroleum products	Occupational exposures to fathers	Not given	Buckley, et al., 1989
	• Gasoline	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

Cancer or Tumor Type	Toxic Exposure	Source of Exposure	Timing or Duration	Reference
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 • 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 • Flea collars • 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 • Alcohols • Lacquer thinner • 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 • 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

Cancer or Tumor Type	Toxic Exposure	Source of Exposure	Timing or Duration	Reference
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