Keep the Sprays Away?
Home Pesticides Linked to Childhood Cancers

Previous studies have suggested a link between pesticide use in the home and childhood hematopoietic tumors, the most common type of childhood cancer. A new epidemiologic study of French children diagnosed with leukemia or lymphoma in 2003 or 2004 suggests that a child has about twice the risk of developing acute leukemia (AL) or non-Hodgkin lymphoma (NHL) if his or her mother used insecticides while pregnant [EHP 115:1787–1793; Rudant et al.].

The researchers interviewed 1,060 children diagnosed within the prior 6 months and 1,681 control children. When analyzing the data on the children, the team controlled for other factors that may alter a child’s risk of getting cancer, including family cancer history and whether the child was breastfed. The children with cancer were part of the French National Registry of Childhood Blood Malignancies, begun in 1990, which documents all children in the country under age 15 year who have had hematopoietic tumors.

The researchers asked the children’s mothers about their use while pregnant of pesticides in their homes, on pets, and in the garden. They also asked about the father’s use of pesticides while the mother was pregnant and after the child’s birth. Just over 50% of the parents who had a child with AL or NHL had used pesticides at least once during the pregnancy, as did just under 40% of the parents of the control group. Children had 2.1 and 1.8 times the risk of developing AL or NHL, respectively, with maternal use of pesticides during pregnancy.

Mothers’ use of insecticides during pregnancy was significantly associated with childhood AL, NHL, and mixed-cell Hodgkin lymphomas (HLs). Use of pesticides by fathers was also related to AL and NHL. The association was stronger for common B-cell acute lymphoblastic leukemia (ALL) and acute myeloblastic leukemia than for T-cell ALL or mature B-cell ALL. It was also stronger for Burkitt lymphoma than for the other NHLs. Of the HLs, the study linked only the mixed-cell subtype to pesticide use. The strength of the association between pesticide use in the home and cancer did not change as the children grew older.

This is the first study to tease out the different types of hematopoietic cancers as they relate to pesticide use in the home. Other studies have found a link between parents’ occupational exposure to pesticides and childhood cancers, but few of the parents in the French study were exposed to pesticides at work or through farming. Whether a family was rural or urban didn’t alter a child’s risk of developing cancer.

The two types of lymphoma associated with maternal pesticide use during pregnancy have also both been linked to the Epstein-Barr virus, which may suggest a link between pesticide exposure and susceptibility to a viral lymphoma. According to the authors, the consistency of the findings suggests pregnant women may want to avoid pesticide use. –Tina Adler

Dietary Dose
Rodent Feed Affects ED Screening Results

As the U.S. EPA begins its program to test endocrine-disrupting effects of pesticides, researchers caution that routine screening methods could distort results [EHP 115:1717–1726; Thigpen et al.]. The team discovered that some commercially available rodent diets can cause early sexual maturation similar to that induced by chemical endocrine disruptors. Furthermore, one rat strain commonly used by many researchers is not the most sensitive to the effects of endocrine disruptors and thus may not provide optimal results.

The U.S. EPA Endocrine Disruptor Screening Program was mandated by Congress in 1996 amid mounting evidence that hormone-mimicking chemicals in the environment alter sexual traits in exposed wildlife. Research suggests these chemicals might also contribute to increases in human male reproductive disorders including poor sperm quality, cryptorchidism, and hypospadias. In June 2007 the U.S. EPA published a list of 73 suspect chemicals for initial screening.

According to the authors of the current study, some rodent diets could distort screening results because they contain high levels of plant estrogens. The phytoestrogens genistein and daidzein are found in the soybeans used in many rodent diets. U.S. EPA guidelines allow a limited amount of genistein and daidzein in the diets of rodents used for screening. The authors report, however, that even approved levels of these compounds are sufficient to adversely impact sexual end points that researchers use to measure endocrine disruption. Furthermore, genistein and daidzein levels vary significantly among different batches of the same diet.

Rats on a diet with the highest genistein and daidzein concentrations reached sexual maturity several days earlier than those fed a different batch of the same diet containing lower levels of the compounds. In addition, rodents on high-calorie diets grew faster and reached sexual maturity earlier than those fed a low-calorie diet.

The researchers measured sexual maturity by observing the day each rodent’s vagina opened. Vaginal opening provides a noninvasive measurement that does not require the animal to be sacrificed. In contrast, sexual maturity is typically measured by uterine weight, which increases at puberty. The results revealed that dietary estrogens had a lesser effect on the vaginal opening day of Sprague-Dawley rats than on Fischer 344 rats or CD-1 mice. This indicates that the latter two species may be more sensitive to exogenous estrogens and thus are preferable for screening.

The authors call on scientists screening suspected endocrine disruptors to choose the most sensitive rodents, to minimize the animals’ exposure to dietary estrogens, and to control their caloric intake. Only then, they write, will scientists obtain results that are the most accurate, reproducible, and easiest to compare among laboratories. –Cynthia Washam
Uranium in Drinking Water
Low Dose Acts as Endocrine Mimic

Uranium, the heaviest naturally occurring element, is well known as a radioactive toxicant capable of damaging the kidneys and DNA. A new study has shown for the first time that uranium also acts as an estrogen mimic in mice at concentrations below the U.S. EPA’s safety limit of 30 µg/L in drinking water [EHP 115:1711–1716; Raymond-Whish et al.]. Other metals, including arsenic, cadmium, lead, and mercury, also are known estrogen mimics.

The researchers manipulated the reproductive status of female mice in several ways. They exposed one group of immature female mice to uranium as they matured, a second group of mature female mice to uranium at environmentally relevant concentrations for 30 days prior to breeding and through gestation, and a third group of female mice to uranium immediately after their ovaries were removed. In a fourth group, they removed the ovaries of female mice, then exposed subgroups of this cohort to either uranium or the synthetic estrogen diethylstilbestrol (DES) alone or in combination with the antiestrogen ICI 182,780. All uranium exposures were via the mice’s drinking water at concentrations of 0.5 µg/L–60.0 mg/L.

Uranium had estrogen-like effects at varying dose ranges throughout the suite of experiments. In the first group, exposure resulted in fewer primary and more secondary ovarian follicles among adult females. In the second group, female pups of exposed dams had significantly fewer small primary ovarian follicles. The researchers conjecture that this primary-to-secondary follicle ratio may lead to fewer ovulated eggs and early-onset menopause. In the ovariectomized mice, the researchers found higher uterine weights and accelerated vaginal opening (indicators of earlier puberty onset). In addition, estrogenic activity was blocked in the mice exposed to ICI 182,780 after DES or uranium exposure.

Stress Reaction
Ozone and Co-pollutants Linked with Oxidation

Past studies have hinted that several air pollutants can cause oxidative stress in people, suggesting one mechanism behind diseases such as lung cancer, asthma, and increased cardiopulmonary illnesses and deaths. The evidence has gained more support with the discovery that chronic exposure to ambient ozone, nitrogen dioxide, or particulates is strongly linked with lipid peroxidation, an indicator of oxidative stress [EHP 115:1732–1737; Chen et al.]. Moreover, more damage was seen at higher pollutant concentrations.

Researchers evaluated two oxidative stress indicators in the blood of 120 University of California, Berkeley, students aged 18 to 22 years. Each student was a lifelong resident of either the Los Angeles or San Francisco area, where they had experienced variable seasonal exposures to pollutants including ozone.

To assess lipid peroxidation, the researchers measured 8-iso-prostaglandins-F₂α (8-iso-PGF), which has been found in several studies to be a useful indicator. To assess total antioxidant capacity, they measured ferric-reducing ability of plasma (FRAP), which has a more limited history as an indicator. Pollutant concentrations were estimated from data at monitoring stations near where the students lived.

The lifelong Los Angeles residents had received much higher average ozone exposure over the course of a lifetime (42.9 ppb versus 26.9 ppb for the San Francisco residents), and 8-iso-PGF was twice as high in these students (195.3 pg/mL versus 97.2 pg/mL). There was also a link between relatively higher ambient ozone concentrations during 2-week and 1-month periods and increased 8-iso-PGF. Neither sex, ethnicity, nor weight affected the results, but there was a wide range in 8-iso-PGF among individuals (17.4–940.7 pg/mL), perhaps due to genetic differences.

The researchers also found a significant link between 8-iso-PGF and increased concentration of nitrogen dioxide or particulates, independent of the effects of ozone.

The FRAP assay showed no significant difference in antioxidant capacity between the residents of the two cities. However, there was a threefold difference among all study subjects in antioxidant capacity, and males had about 23% more antioxidant capacity than females.

Although acknowledging that much more study of other populations and locations needs to be done with more precise measures of personal pollutant exposure, the researchers conclude that each of the three pollutants studied can significantly increase oxidative stress. They also report that 8-iso-PGF is an accurate indicator of oxidative stress, while noting that other indicators, such as cytogenetic damage, may also prove useful.

–Bob Weinhold