OP Pesticides in Children's Bodies

The Effects of a Conventional versus Organic Diet

Conventional agriculture includes the use of pesticides to control insects in vegetable, fruit, wheat, and other crops, so it's no surprise that foods derived from these crops can therefore contain pesticide residues. What's in question, though, is what these exposures amount to in terms of body burden. Risk-defining data are lacking, and scant data exist on diet-derived pesticides levels in children's bodies. Now researchers from Seattle and Atlanta characterize the relationship between eating a diet of conventionally grown food products and the amount of organophosphorus (OP) pesticide residues that make it into children's bodies [***EHP* 114:260–263**].

According to a 1993 National Research Council report titled *Pesticides in the Diets of Infants and Children*, diet delivers the bulk of children's exposure to pesticides. This exposure poses a greater health risk to children as compared to adults, because not only do children consume more food on a per-weight basis than adults and consequently have higher exposure, they also may be more vulnerable to the effects of toxicants because they are still developing.

The researchers employed a longitudinal design in which 23 children aged 3 to 11 years accustomed to eating a conventional diet switched to organic foods and back again during a 15-day study period. For the first three days, the children consumed their regular conventional diets. During the next five days, they substituted organic equivalents of their usual plant-derived food items (including fresh produce, juice, processed fruits and vegetables, and grain-based products). For the last seven days, they resumed their conventional diets. Each day, for the entire 15-day period, parents collected a urine sample in the morning when the children woke and again at bedtime.

The urine samples were analyzed for metabolites of several OP pesticides. The most commonly detected metabolites were MDA (a metabolite of malathion) and TCPY (a metabolite of chlorpyrifos). During both conventional phases, 60% of samples contained MDA, and 78% of samples contained TCPY. When children switched to organic foods, the percentage of samples containing MDA dropped to 22% and the proportion with TCPY fell to 50%.

Average concentrations of MDA and TCPY also were significantly lower during the organic phase compared to the conventional phases. During the two conventional phases, mean urinary MDA concentrations were 2.9 and 4.4 micrograms per liter (μg/L) compared with 0.3 μg/L in the organic phase. The mean TCPY level decreased from 7.2 to 1.7 μg/L between the first and second phases, and rose to 5.8 μg/L when the children resumed their conventional diets.

Metabolite levels varied widely among the samples, however. Recent research suggests that fractions of MDA and TCPY form as the parent compounds degrade in foods and the environment. Therefore, some proportion of the children's exposure may have been to the metabolites themselves in the foods.

The current study provides insight into how residual OP pesticides in food correspond with the absorbed dose, and the researchers conclude that a diet of organic foods protects children from exposure. They caution against applying results to the general population, however. Given that people from different backgrounds and living in different areas may have different and more significant OP exposures, it would be a mistake to assume that switching to an organic diet would eliminate all exposure to these pesticides. The study does support the National Research Council's conclusion that dietary intake is a major source of OP pesticide exposure, but some children may receive even more exposure from the use of pesticides in the home, and further research is needed. **–Julia R. Barrett**

No beef here. A study of organophosphate metabolites in children eating an alternating conventional/organic/conventional diet shows that eating organic plant-derived foods really can reduce pesticide exposure.

PhotoAlto

Endocrine Disruption and Flame-Retardant Chemicals

PBDE-99 Effects on Rat Sexual Development

Chemical flame retardants containing polybrominated diphenyl ethers (PBDEs) have attracted growing attention in recent years from toxicologists. Unlike their chemical cousins, dioxins and polychlorinated biphenyls (PCBs), environmental levels of PBDE compounds are increasing, as are concentrations found in human breast milk. This is of concern because of the potential that PBDEs may cause developmental toxicity due to endocrine-modulating effects, as has previously been documented with dioxins and PCBs. Results of a new German study examining developmental exposure in rats to a commonly used and environmentally abundant PBDE compound, PBDE-99,

lend support to suspicions that PBDEs can have detrimental effects on sexual development in the offspring of exposed mothers [***EHP* 114:194–201**].

The researchers examined sexual development end points—circulating sexual steroid concentrations, reproductive organ development, and sexually dimorphic behavior—that have been shown in similar rodent experiments to change following exposure to a mixture of PCBs reconstituted according to the congener pattern found in human breast milk. In the current study, weight-matched groups of dams received daily subcutaneous injections of PBDE-99 from gestational days 10 through 18 at doses of 1 or 10 milligrams per kilogram body weight (mg/kg). For comparison, another group was dosed with 30 mg/kg of the PCB mixture Aroclor 1254 (A1254).

In PBDE-exposed male offspring, pronounced decreases in circulating sex steroids (estradiol, testosterone) were seen both at weaning and in adulthood. Anogenital distance, an androgen-dependent marker of sexual development, was also reduced in the male offspring. The males further displayed a dose-dependent increased preference for sweets, which is a sexually dimorphic behavior in rodents—this finding indicates feminization in the males. A slight acceleration in onset of puberty was noted in the low-dose group.

The PBDE-exposed females had less severe effects. Onset of puberty was mildly delayed in the high-dose group. Also, the number of primordial/primary (rudimentary) ovarian follicles was reduced in the low-dose group, with a more pronounced decline in secondary (more developed) follicles within the high-dose group. These results could indicate an impaired reproductive life span, in that ovarian follicles are a key indicator of ovarian health. The females also had an insignificant increase in sweet preference.

The researchers found no effect on sweet preference in male or female offspring exposed to the PCB mixture, but in the females they did see a significant increase in the number of tertiary (still larger, more developed) follicles. The exposure also adversely affected steroid concentrations in males and sexual development in both sexes. Thus, it appears that the pattern of endocrine-disruptive effects differs for PBDE-99 and A1254, which may be due to the higher content of dioxin-like compounds in the PCB mixture.

The scientists also examined organ weights as an indicator of overall development in the rodents. They found that pituitary gland weights were slightly decreased in males in the PBDE-99 high-dose group at weaning, while they were increased in females in the low-dose group. The authors speculate that these effects may indicate a biphasic response to PBDE-99, and suggest that the phenomenon should be studied further in future research. Results also included a marked dose-dependent decrease in thyroid gland weight in adult rats of both sexes exposed to either PBDE-99 or A1254.

This study adds to a growing body of literature indicating that chemical flame retardants are endocrine-disrupting compounds with the potential to profoundly affect sexual development and sexually dimorphic behaviors. The fact that several effects were seen in adulthood, long after termination of the exposure, indicates that the rats' gestational exposure caused permanent physiologic damage. With increases in human body burden and environmental levels, and with the compounds' apparent persistence in both venues, it is safe to assume that PBDEs will be the focus of more urgent research activity. **–Ernie Hood**

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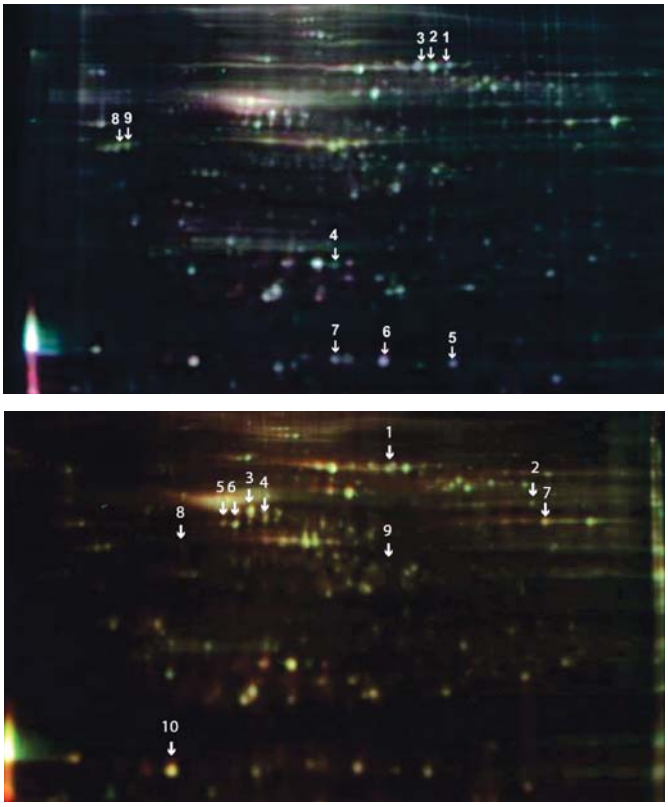


Lights in the darkness. 2D-DIGE reveals nine striatal proteins (top) and ten hippocampal proteins (bottom) that may serve as biomarkers of early-stage PBDE-99 toxicity.

Proteomic Insights into Brain Development

Neurotoxic Effects of PBDE-99 in Mice

The amounts of polybrominated diphenyl ethers (PBDEs) found in human tissues, particularly breast milk, are rising steadily. PBDEs are flame retardants that reduce fire risks when added to electronic equipment and household products. Epidemiologic studies have yet to show conclusive evidence of PBDE toxicity in humans. However, studies in animals have shown these chemicals to produce effects such as liver damage, altered thyroid hormone levels, developmental changes, and neurotoxicity. In the present study, a Swedish team uses proteomic methods to investigate the early-stage neurotoxic effects of PBDE-99 on two parts of the developing mouse brain: the striatum and the hippocampus [***EHP* 114:254–259**]. The findings help deconstruct the mysterious mechanisms that underlie PBDE-99 neurotoxicity.

The striatum and the hippocampus are both part of the cholinergic and monaminergic systems, which play roles in neurotransmitter functioning and other aspects of cognition. The authors sought specifically to uncover PBDE-induced cellular events leading from the neonatal brain growth spurt to permanent neurological problems in adult animals.

PBDE-99 is among the most common PBDE congeners found in environmental and human tissue samples. This penta-brominated

compound impairs spontaneous behavior and habituation among adult mice exposed neonatally to moderate doses. These effects are progressive, worsening with age.

During the study, 10-day-old mice of both sexes were given a single dose of 12 milligrams PBDE-99 per kilogram body weight. After 24 hours, the mice were sacrificed, their brains dissected, and the striatum and hippocampus isolated for study. The team used 2D-DIGE to compare protein expression patterns between treatment and control groups. The analysis illuminated 40 proteins in the striatum and 56 proteins in the hippocampus whose expression was altered by PBDE-99 exposure.

From this initial grouping, nine striatal proteins and ten hippocampal proteins were selected for identification using MALDI-ToF-MS. Among the striatal proteins affected by PBDE-99 were several (including Gap-43/neuromodulin and stathmin) that participate in neurodegeneration and neuroplasticity. The affected hippocampal proteins (including α-enolase, γ-enolase, Atp5b, and α-synuclein) tend to participate in metabolism and energy production. Many of these proteins are linked to protein kinase C, a signaling molecule whose role in development and function, as well as in learning and memory, has been intensively studied.

Based on these findings, the authors conclude they have identified potential protein biomarkers that reflect the immediate consequences of early-stage PBDE-99 toxicity, in addition to the processes that drive its neurological effects in older animals. The researchers suggest that protein kinase C signaling is a target of PBDE-99 toxicity in the developing mouse brain. Moreover, the authors propose that neonatal cell stress induced by PBDE-99 exposure, in addition to related neurodegenerative processes and aberrant neuroplasticity, may contribute to the latter-stage behavioral effects observed in adult mice. The responses within the striatum and hippocampus differ, however, reflecting the underlying heterogeneity between different brain parts and cell populations. **–Charles W. Schmidt**

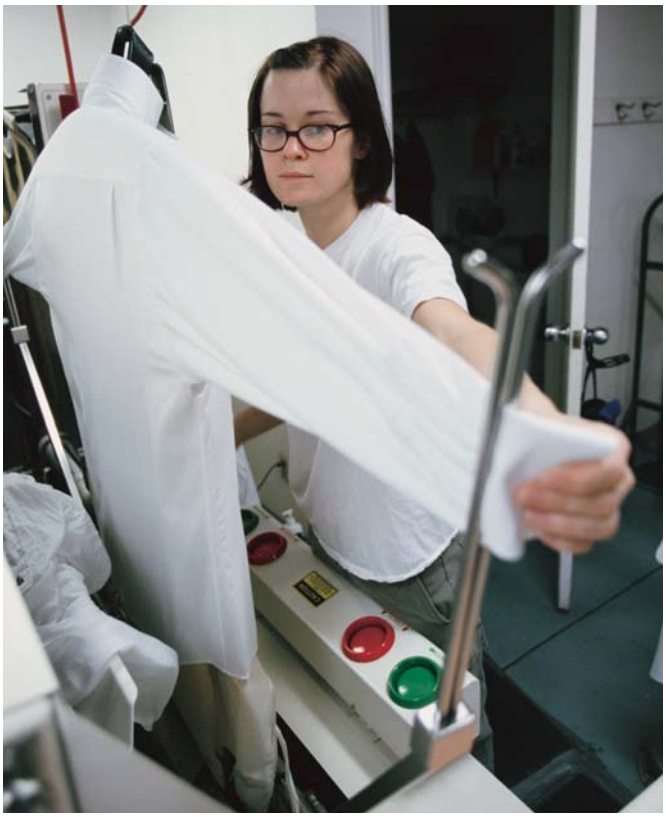
Pressed for Hard Facts

Multiple Tetrachloroethylene–Cancer Links Go Unconfirmed

Recent U.S. studies have linked dry cleaners' exposure to tetrachloroethylene, a solvent used in the industry, to an increased risk for a number of cancers, including esophageal, lung, and cervical cancer. Results of other studies on bladder and pancreatic cancer are equivocal. Still other studies have shown an increased risk of non-Hodgkin lymphoma. Now a study by a team of Nordic researchers of cancer risk among dry-cleaning workers in Denmark, Finland, Norway, and Sweden finds that, with the exception of bladder cancer, exposure to the solvent showed no link to the disease [***EHP* 114:213–219**].

The researchers identified 46,768 dry-cleaning and laundry workers from the 1970 censuses in the four countries. The investigation was a series of case–control studies nested within this cohort of workers. Controls were matched by country, sex, and five-year group for age and year of cancer diagnosis. The team studied the period from 1964 to 1979, when tetrachloroethylene was the primary solvent used for dry cleaning in these countries.

The team considered four categories of exposure: exposed workers in dry-cleaning shops with fewer than ten workers (reflecting a probability of sharing tasks and working in more cramped quarters), other workers in dry-cleaning shops (such as seamstresses and office workers), unexposed laundry workers and others not working in a dry-cleaning shop, and those who could not be classified.



Clean sweep for dry cleaners? Tetrachloroethylene, a solvent widely used in the dry-cleaning industry, has been implicated in many cancers, but a new study of Nordic dry cleaners fails to corroborate most of those links.

Blinded telephone interviews were done with cases, controls, and, eventually, next of kin in Norway and Sweden. If the subject's occupation was dry cleaning, the interview covered length of employment in the dry-cleaning shop, number of workers in the shop, solvents used, and the subject's smoking and drinking habits. For Denmark and Finland, pension records and other data sources were used to gather comparable information.

Although exposure to tetrachloroethylene varied greatly among shops, the average annual level of exposure was fairly stable between 1964 and 1979. The team found no increase in risk of cancers of the esophagus, gastric cardia, liver, pancreas, or kidney. There was also no link to non-Hodgkin lymphoma. The study did, however, find a 44% excess risk in bladder cancer concentrated in Norway and Denmark, the two countries with the best data.

The authors point to several strengths of the study, particularly its completeness. It covered all persons working in dry cleaning in 1970 in the Nordic countries. It also compared two cohorts, dry-cleaning workers and laundry workers, who had similar jobs except for the exposure to tetrachloroethylene.

The authors also acknowledge the study had some weaknesses. For a high proportion of cases and controls from Sweden and Finland the authors could not determine whether the subjects worked in either a laundry or dry-cleaning business. Consequently, estimates of cancer risk were reported for all four countries together and for Denmark and Norway together. Furthermore, subjects could not be classified by exposure level to tetrachloroethylene. The researchers note, though, that because the data indicated a fairly stable level of exposure during employment, they consider length of time on the job an adequate surrogate measure of a cumulative dose. **–Harvey Black**

Rubberball