**Thyroid Hormone Understanding Branches Out Insights into PBDE Impacts on Brain Development**

Polybrominated diphenyl ether (PBDE) flame retardants and their hydroxylated metabolites are structurally similar to thyroid hormone. A detailed study now provides one of the most insightful assessments to date of how environmentally relevant levels of PBDEs may impair brain development by interfering with thyroid hormone receptor (TR)–mediated transcription [EHP 119(2):168–175; Ibhazehiebo et al.]

PBDEs were used for decades as flame retardants in a wide variety of consumer and household goods, and U.S. citizens are widely exposed to them. Scientists know that PBDEs can cross the blood–brain barrier and accumulate in the central nervous system, and a growing body of evidence implicates these chemicals as developmental neurotoxicants. PBDEs and their metabolites have been detected in fetal blood, liver, and placenta, and in human milk.

Thyroid hormone deficiency in the perinatal period can cause abnormal brain development. The study authors studied how PBDEs affected the mechanisms underlying thyroid hormone action in the developing brain using an established rodent cerebellum model. The experiments were designed to distinguish between effects on TR-mediated gene transcription due to 1) altered interactions between thyroid hormone and the TR and 2) altered interactions between the TR and short DNA sequences known as thyroid hormone response elements (TREs).

**Beastly Beauty Products Exposure to Inorganic Mercury in Skin-Lightening Creams**

The most common exposure to mercury is from organic methylmercury found in fish. People with no workplace exposure to mercury typically have low levels of exposure to organic or elemental mercury, although nonoccupational exposure can occur from dental amalgams, some herbal medicine products, and cosmetics that contain mercury. When a New York City (NYC) biomonitoring study revealed that thousands of women in that city may have been exposed to dangerous levels of inorganic mercury from imported skin-lightening creams, city health officials enlisted the help of U.S. and international health agencies in getting the creams off local store shelves [EHP 119(2):203–209; McKelvey et al.]

In 2004 the NYC Department of Health and Mental Hygiene (DOHMH) conducted the nation’s first local Health and Nutrition Examination Survey. Analysis of urine specimens from 1,840 adult New Yorkers collected during the survey yielded a geometric mean mercury concentration of 0.73 µg/L, slightly higher than the national average of 0.5 µg/L. The authors took note when 13 women were found to have urine mercury concentrations exceeding the state’s reportable level of 20 µg/L; 4 women had levels exceeding 50 µg/L.

All 13 highly exposed women were Hispanic or black, and 10 had been born in the Dominican Republic. Each of the 9 women interviewed on followup had used mercury-containing skin-lightening cream. One such product sampled by DOHMH workers contained 6,190 ppm mercury. The U.S. Food and Drug Administration (FDA) limit for mercury in skin-care products is 1 ppm.

Extrapolating from the population sampled, the authors estimate nearly 27,000 New Yorkers may have urine mercury levels exceeding 20 µg/L. Although the researchers did not assess potential health effects among the highly exposed women, occupational studies indicate kidney and neurologic toxicity may occur when urine mercury levels exceed 20 µg/L.

City health officials responded to the survey results by seizing 12 brands of illegally imported cosmetics from store shelves. All the products listed mercury as an active ingredient. Press releases issued by the DOHMH urged residents to report mercury-tainted cosmetics and the shops selling them, and New Jersey investigators were enlisted to plug the pipeline to importers in that state. The Pan American Health Organization called on the Dominican Republic to stop manufacturing the dangerous products. The Dominican Secretary of Health reportedly has notified all laboratories to stop manufacturing mercury-containing skin-care products.

The authors realize some tainted products may still cross the border, as they have for years despite FDA prohibitions. But they believe their efforts, coupled with evidence of mercury’s toxicity and continued vigilance, will substantially reduce the availability and use of these products.

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The scientists initially expected to demonstrate that PBDEs displaced thyroid hormone from the TR site. Instead they found PBDEs may prevent the TR from interacting with TREs, possibly through effects on the TR DNA-binding domain that normally binds to TREs in thyroid hormone–regulated genes.

The team identified two PBDE compounds, BDE-209 and BDE-100, as playing important roles in suppressing transcription from several TREs. None of the hydroxylated PBDE metabolites evaluated significantly suppressed TR-mediated transcription.

Decreases in thyroid hormone levels have been shown to alter the complex treelike branching of Purkinje cell dendrites, which is critical to normal brain development. The authors previously reported effects of polychlorinated biphenyls on dendrites that they determined were mediated by effects on the TR. The current study showed the action of BDE-209 on TR-mediated transcription also inhibited the growth and branching, or arborization, of Purkinje cell dendrites. These effects may disrupt other aspects of brain development, given that TR-mediated gene expression occurs in many other cells.

The scientists say their work also suggests the effects they observed are associated with additional pathways, such as disruption of intracellular signaling pathways that rely on calcium ion homeostasis. It is unknown how many genes have TREs; therefore, the new work indicates an important next step will be to unearth the mechanism by which PBDEs can disrupt or suppress those TRE-mediated development genes.

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**Heat Effects Are Unique**

**Mortality Risk Depends on Heat Wave, Community Characteristics**

During heat waves, higher-than-normal temperatures can present a deadly threat, with mortality occasionally doubling. Recent studies have demonstrated that heat-related mortality risk is influenced by the characteristics of the individual heat wave (such as heat intensity, duration, and timing in season). Researchers explored this relationship more fully in one of the largest multi-city studies to date of heat wave impacts in the United States [*EHP* 119(2):210–218; Anderson and Bell].

The authors identified heat waves in 43 U.S. communities during the years 1987–2005. A heat wave was defined as 2 or more days in which temperatures exceeded the 95th percentile of warm season (May–September) temperatures for that community during the 19-year period. Each heat wave was characterized according to heat intensity (average mean temperature), duration in days, and the point in the season when the heat wave occurred.

The investigators estimated a 3.74% increase in average daily risk of nonaccidental death during the heat waves compared with non–heat wave days. Although longer and more intense heat waves were more common in the South, estimated effects of heat waves on mortality were greater in the Midwest and greatest of all in the Northeast. The authors attribute this phenomenon to Southern residents being perhaps more physiologically and behaviorally adapted to extreme temperatures. Nationwide, heat waves that occurred earlier in the warm season appeared to have a greater effect on mortality than heat waves occurring later (an average 5.04% increase compared with an average 2.65% increase), as did hotter or longer heat waves.

Considering that heat waves are expected to become more common and intense in some areas as the Earth’s climate changes, it is important to understand the factors that make individual communities vulnerable to heat-wave effects and that make individual heat waves more likely to cause excess deaths. The authors conclude it is important for officials to develop local response plans on the basis of heat-wave mortality trends in their own communities; when it comes to planning for health effects of heat waves, one size does not fit all.

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