

## Maternal exposure to polybrominated and polychlorinated biphenyls: Infant birth weight and gestational age

Marjory L. Givens<sup>a,b</sup>, Chanley M. Small<sup>a</sup>, Metrecia L. Terrell<sup>a</sup>, Lorraine L. Cameron<sup>c</sup>, Heidi Michels Blanck<sup>d</sup>, Paige E. Tolbert<sup>a,b</sup>, Carol Rubin<sup>e</sup>, Alden K. Henderson<sup>f</sup>, Michele Marcus<sup>a,b,\*</sup>

<sup>a</sup> Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA

<sup>b</sup> Department of Environmental and Occupational Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA

<sup>c</sup> Environmental and Occupational Epidemiology Division, Michigan Department of Community Health, Lansing, MI, USA

<sup>d</sup> Division of Nutrition and Physical Activity, NCCDPHP, Centers for Disease Control and Prevention, Atlanta, GA, USA

<sup>e</sup> National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA, USA

<sup>f</sup> Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention, Atlanta, GA, USA

Received 13 December 2006; received in revised form 8 May 2007; accepted 14 May 2007

Available online 6 July 2007

### Abstract

Understanding the influence of maternal exposures on gestational age and birth weight is essential given that pre-term and/or low birth weight infants are at risk for increased mortality and morbidity. We performed a retrospective analysis of a cohort exposed to polybrominated biphenyls (PBB) through accidental contamination of cattle feed and polychlorinated biphenyls (PCB) through residual contamination in the geographic region. Our study population consisted of 444 mothers and their 899 infants born between 1975 and 1997. Using restricted maximum likelihood estimation, no significant association was found between estimated maternal serum PBB at conception or enrollment PCB levels and gestational age or infant birth weight in unadjusted models or in models that adjusted for maternal age, smoking, parity, infant gender, and decade of birth. For enrollment maternal serum PBB, no association was observed for gestational age. However, a negative association with high levels of enrollment maternal serum PBB and birth weight was suggested. We also examined the birth weight and gestational age among offspring of women with the highest (10%) PBB or PCB exposure, and observed no significant association. Because brominated compounds are currently used in consumer products and therefore, are increasingly prevalent in the environment, additional research is needed to better understand the potential relationship between *in utero* exposure to brominated compounds and adverse health outcomes.

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**Keywords:** Maternal exposures; Infant health; Environmental toxicants; Gestational age; Birth weight; PBB; PCB

### 1. Introduction

Infant gestational age and birth weight are reflective of developmental progression from the time of conception to birth, and also are associated with various health out-

comes in later life. For those infants born pre-term or of low birth weight, there is a heightened risk of morbidities, including developmental disabilities and chronic conditions, and mortality (McCormick, 1985; Kramer et al., 2000; Kramer, 2003). While the proportion of infants born of low birth weight in developed countries has declined (Kramer, 2003), the overall number of pre-term births is on the rise in industrialized nations (Johnston et al., 2001).

Maternal exposures during gestation can influence the structural and functional development of the fetus. A wide

\* Corresponding author. Address: Department of Epidemiology, Rollins School of Public Health, Emory University, 1518 Clifton Road, NE, Atlanta, GA 30322, USA. Tel.: +1 404 727 8010; fax: +1 404 727 8737.

E-mail address: [mmarcus@sph.emory.edu](mailto:mmarcus@sph.emory.edu) (M. Marcus).

range of factors, including low maternal socio-economic status, lack of prenatal care, and smoking, have been associated with infants born pre-term or of low birth weight (Kramer, 2003; Knackstedt et al., 2005). Due to the heightened sensitivity of the fetal life stage, the fetus is extremely vulnerable to environmental challenges, whether endogenous to the mother, external biological agents, or synthetic compounds.

Brominated flame retardants are relatively ubiquitous in the environment. These halogenated organic compounds are supplemental agents in a variety of consumer products, including electronic appliances, automotive parts, furniture, textiles, and plastic foams, intended to reduce fire-related injuries and property damage (Birnbaum and Staskal, 2004). Although these compounds have been recognized for their utility, the possible consequences for human health have been described in the scientific literature (Anderson et al., 1979; Landrigan et al., 1979; Meester, 1979; Rosenman et al., 1979; Silva et al., 1979; Stross et al., 1979; Valciukas et al., 1979; Wolff et al., 1979a,b; Bahn et al., 1980; Weil et al., 1981; Chanda et al., 1982; Kreiss et al., 1982; Eyster et al., 1983; Seagull, 1983; Jacobson et al., 1984; Lipson, 1987; Hoque et al., 1998; Blanck et al., 2000a,b, 2002; Sweeney et al., 2001; Birnbaum and Staskal, 2004). Moreover, production of these compounds has increased dramatically over the last 20 years, and there is an increasing prevalence of exposure to brominated flame retardants worldwide (Birnbaum and Staskal, 2004).

Polybrominated biphenyls (PBB) constitute a class of compounds that were once marketed for use as a flame retardant. A mixture of persistent organic congeners with lipophilic properties (ATSDR, 2004), PBB congeners are resistant to degradation and are stored in adipose tissue. In 1973, this halogenated organic mixture contaminated the food source of numerous Michigan communities due to an inadvertent replacement of a nutritional supplement, NutriMaster, with FireMaster in cattle feed.

The production of PBB ceased in 1979; however, the environmental and human health consequences of exposure are still being documented. Because PBB congeners added to consumer products are not covalently bound (ATSDR, 2004), PBB congeners are continually released into the environment and have the potential to contaminate ecosystems years after their production has ceased. Exposure to PBB has been associated with adverse effects on the endocrine, immune and neurological systems (Landrigan et al., 1979; Meester, 1979; Silva et al., 1979; Weil et al., 1981; Lipson, 1987; Hoque et al., 1998; Blanck et al., 2000a,b, 2002).

Polychlorinated biphenyls (PCB) are related halogenated organic compounds, comprised of over 200 congeners, once used as lubricants or coolants in electrical equipment. Not unlike the cessation of PBB production, manufacturing of PCB was also banned in North America and other industrialized countries in the 1970s (ATSDR, 2000). The primary pathway of exposure to PCB in the

general population is through the food chain, with the most noted being fish consumption. Fish consumed from the PCB-contaminated waters of the Great Lakes have been identified as a heightened source of dietary exposure (ATSDR, 2000). The adverse human health outcomes associated with PCB exposure include dermal anomalies, endocrine disruption, neurobehavioral disorders, and an impaired immune system (for review see (Ross, 2004)).

Several experimental animal studies indicate that PBB and PCB can cross the placental barrier (Eyster et al., 1983; Jacobson et al., 1984; Guvenius et al., 2003; ATSDR, 2004) and *in utero* PBB exposure results in reduced fetal birth weight and shortened gestational period (Corbett et al., 1975; Harris et al., 1978; Lambrecht et al., 1978; Aulerich and Ringer, 1979; McCormack et al., 1981). Evidence from studies of related halogenated organics, such as PCB, and DDT (1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane), suggests that *in utero* exposure to these agents is associated with infants born pre-term (Longnecker et al., 2001) and of low birth weight (Fein et al., 1984; Baiberge-nova et al., 2003). Thus, there is reason to believe that exposures to PBB *in utero* may adversely affect the developing infant. Given the temporal trends in premature births, and the ubiquitous presence of halogenated organics, the present study examines the potential association between exposure to PBB and PCB *in utero* and infant birth weight and gestational age.

## 2. Research methods and study design

### 2.1. Study population

The contamination of the Michigan food chain with the fire retardant, FireMaster, exposed thousands of residents to PBB. In an effort to understand the consequences of this exposure, the Michigan Department of Community Health (MDCH), in collaboration with the US Public Health Service, organized a prospective cohort study in 1976, which enrolled almost 4000 men, women and children who had consumed contaminated food products. Information regarding the incident and the registry cohort has been previously described (Carter, 1976; Landrigan et al., 1979; Meester, 1979; Fries, 1985). Follow-up interviews by telephone, termed the 1997 Michigan Female Health Study, were conducted from 1997 to 1998 with 1185 women at least 18 years of age from the original cohort (Thomas et al., 2001; Kaiser et al., 2003). Five hundred seventy-eight of these participants were mothers who consented to release birth certificate information for their children. Of these women, 493 conceived and gave birth from 1973 to 1997 to infants who were potentially exposed *in utero*. A serum PBB measure was available for 450 of these mothers.

Electronic birth certificate information was obtained for 925 infants born to the 450 mothers. Twenty-six infants were excluded due to the following: gestational age less

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